



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 1 of 64  
Atty. Dkt.: 2551-69

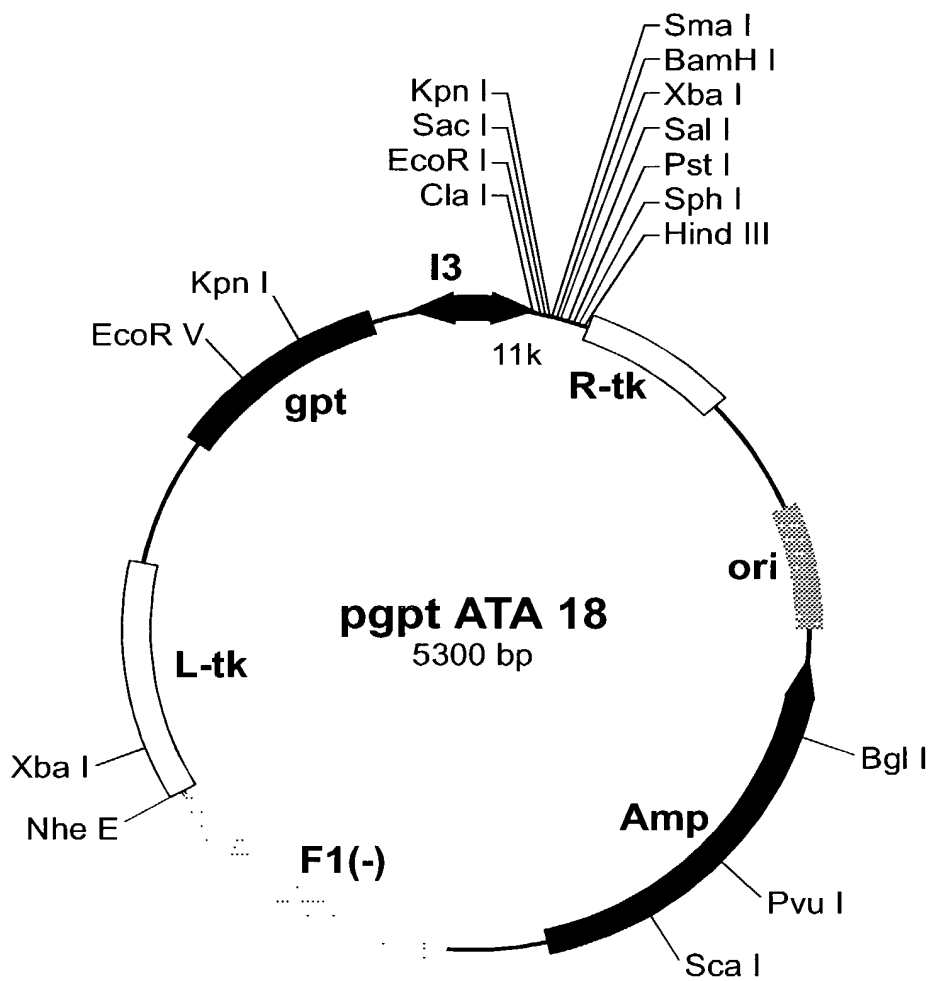


Figure 1



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 2 of 64  
 Atty. Dkt.: 2551-69

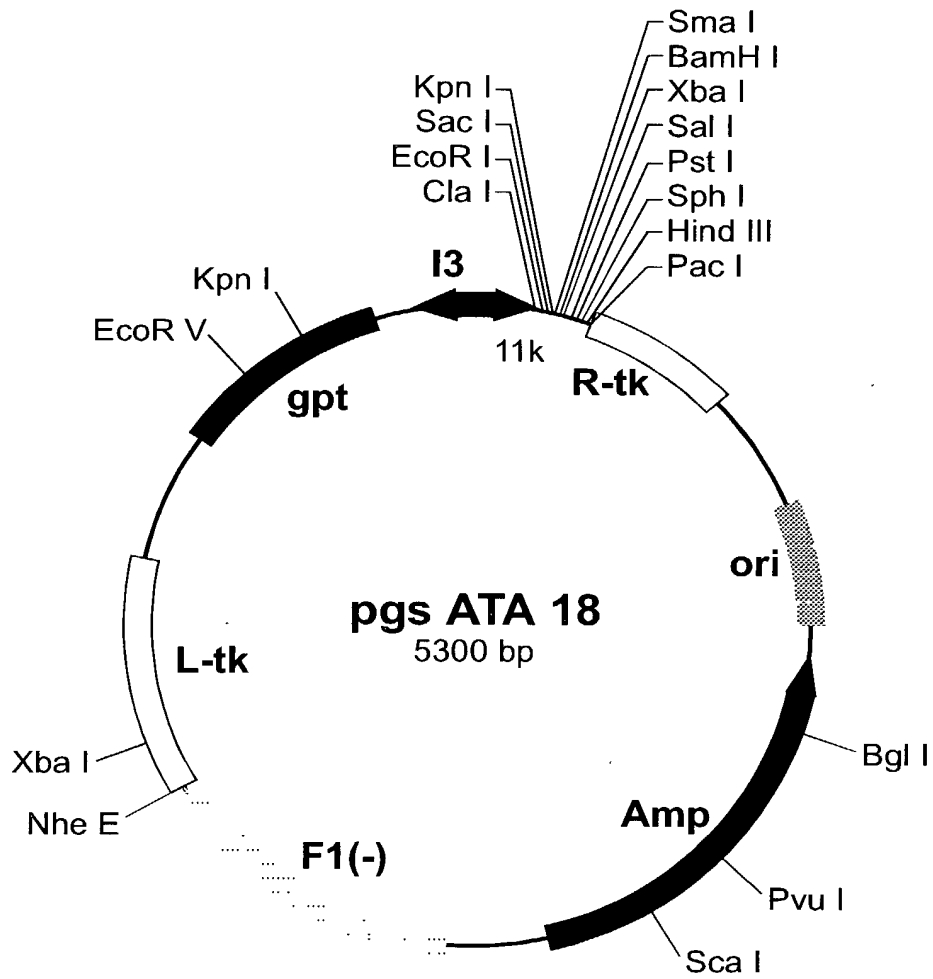


Figure 2



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 3 of 64  
 Atty. Dkt.: 2551-69

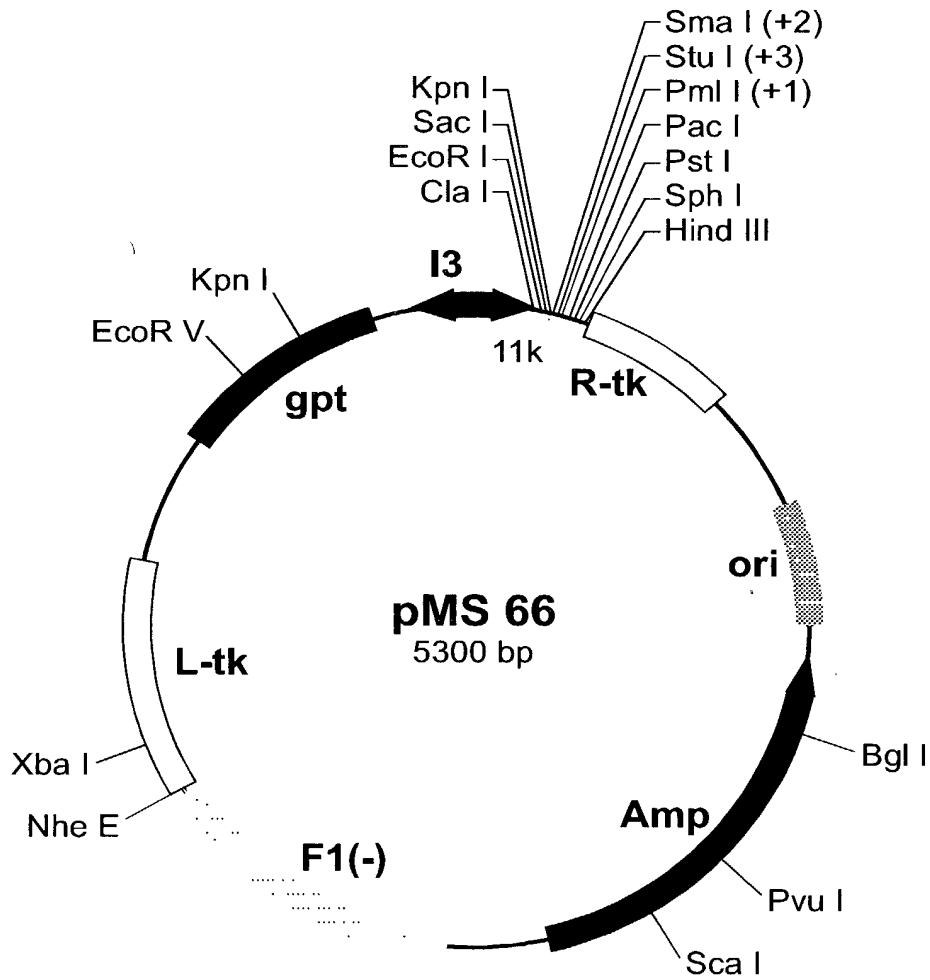


Figure 3

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 4 of 64  
Atty. Dkt.: 2551-69

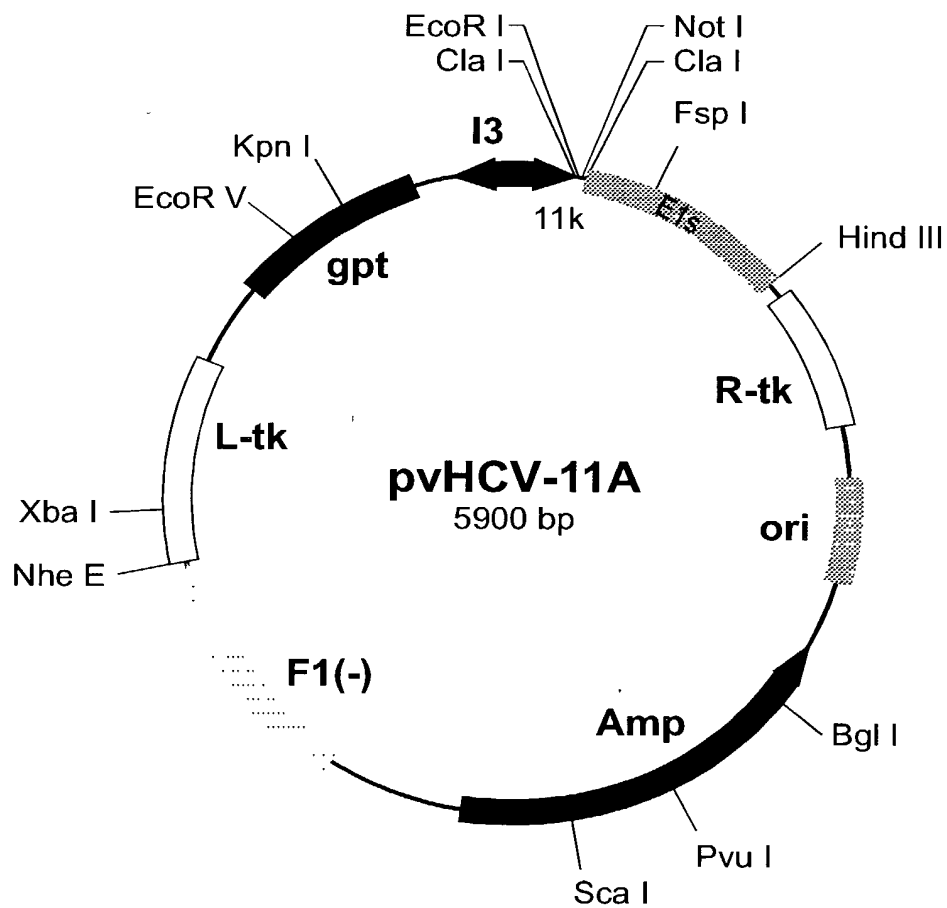


Figure 4

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 5 of 64  
 Atty. Dkt.: 2551-69



# Anti-E1 levels in NON-responders to IFN treatment

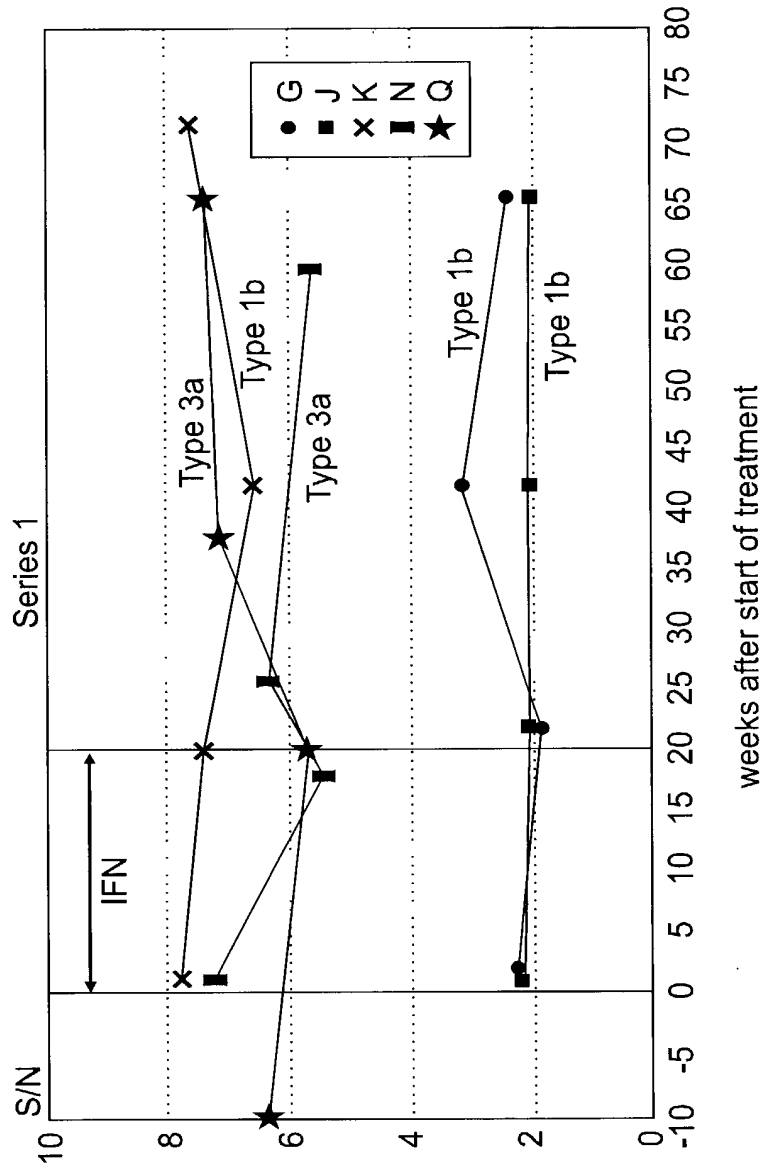


Figure 5



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 6 of 64  
Atty. Dkt.: 2551-69

# Anti-E1 levels in RESPONDERS to IFN treatment

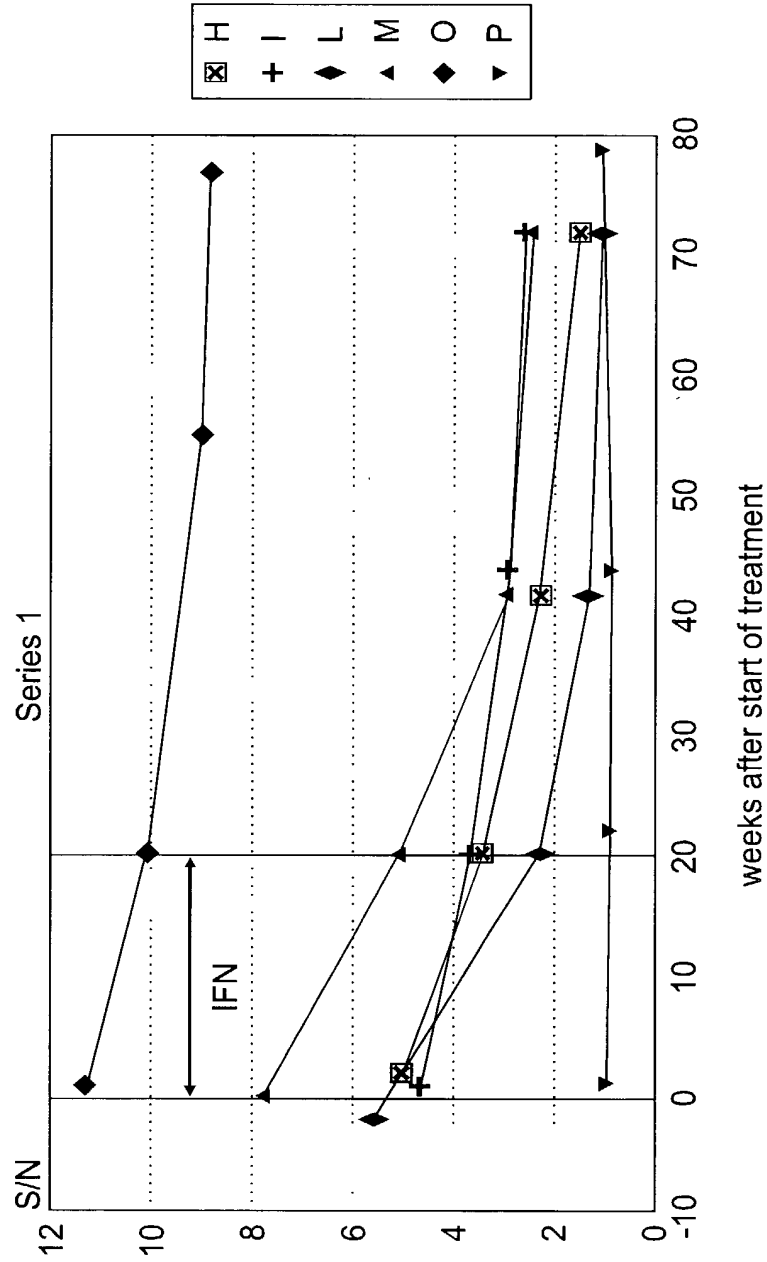


Figure 6

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 7 of 64  
 Atty. Dkt.: 2551-69



# Anti-E1 levels in patients with COMPLETE response to IFN

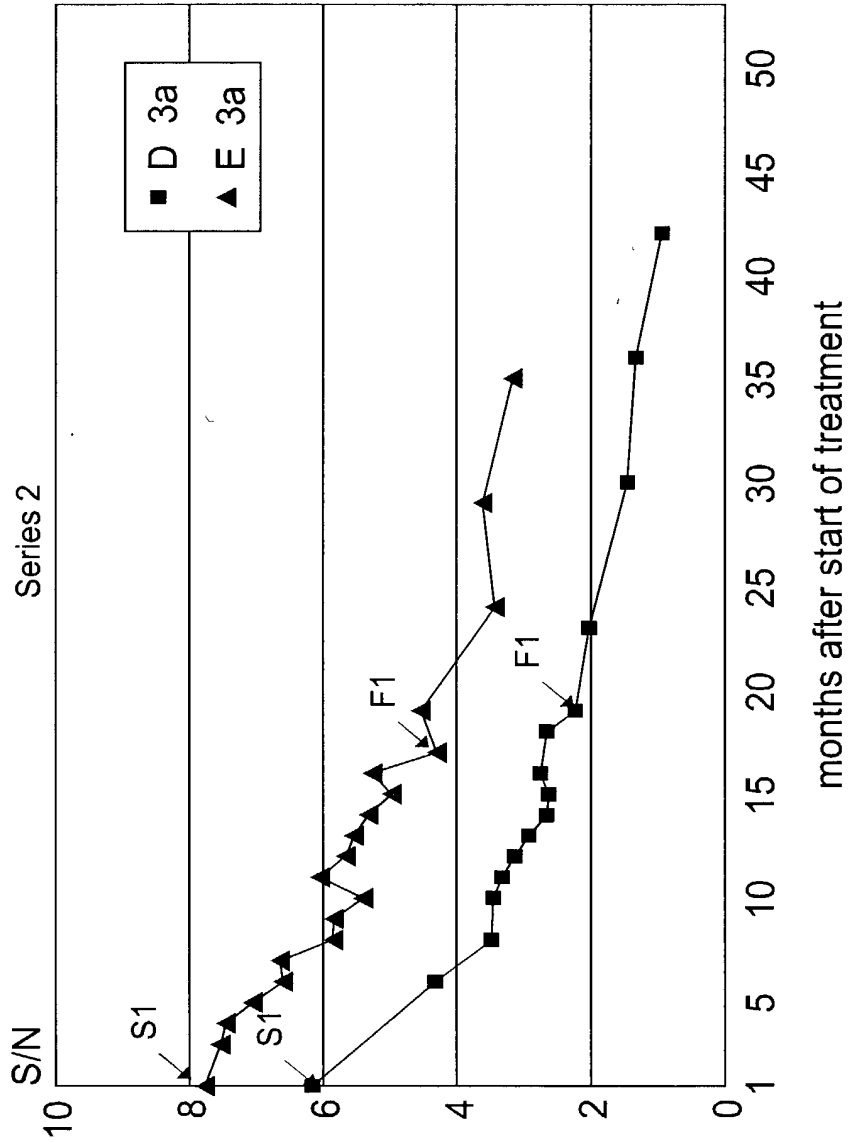
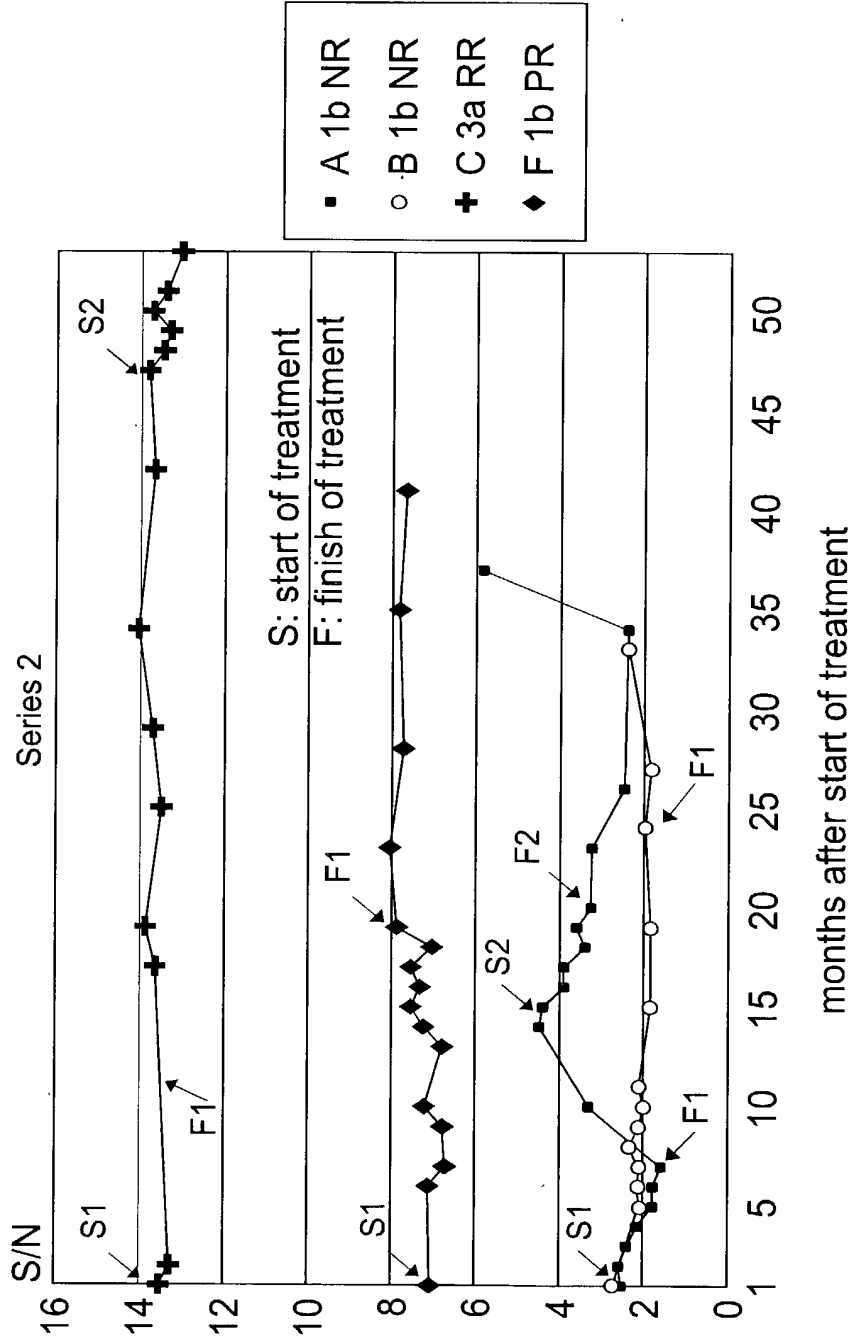


Figure 7



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 8 of 64  
Atty. Dkt.: 2551-69

# Anti-E1 levels in INCOMPLETE responders to IFN treatment





Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 9 of 64  
Atty. Dkt.: 2551-69



# Anti-E2 levels in RESPONDERS to IFN treatment

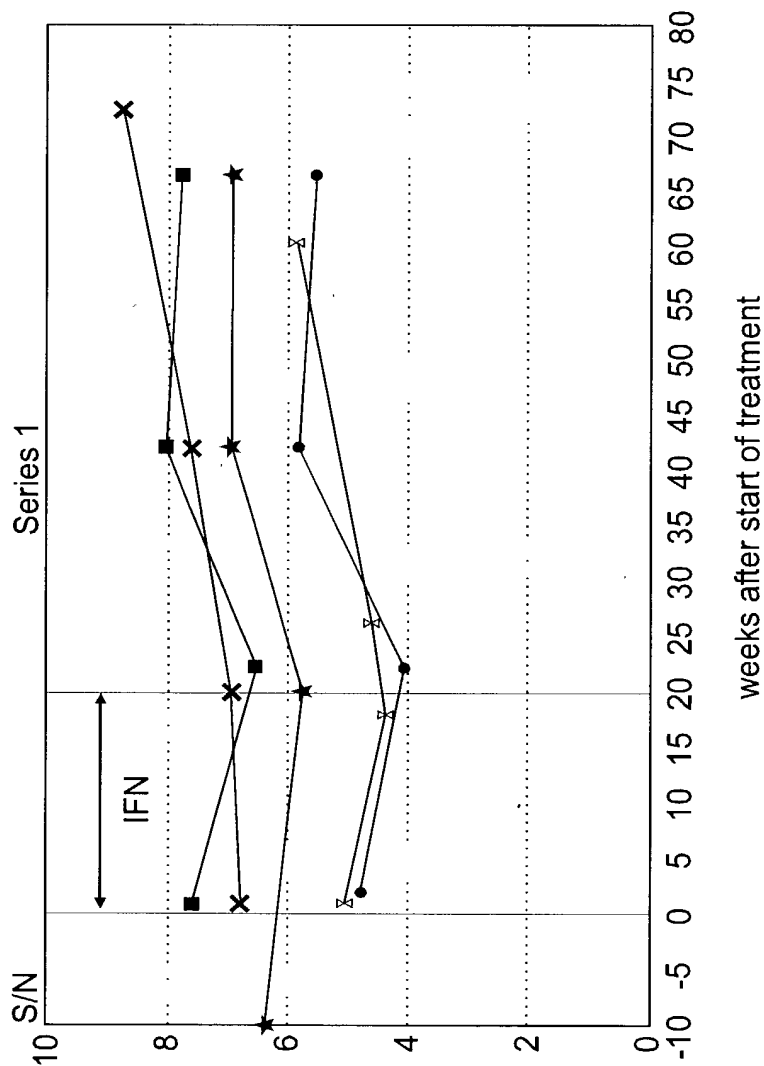


Figure 9



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 10 of 64  
Atty. Dkt.: 2551-69

# Anti-E2 levels in RESPONDERS to IFN treatment

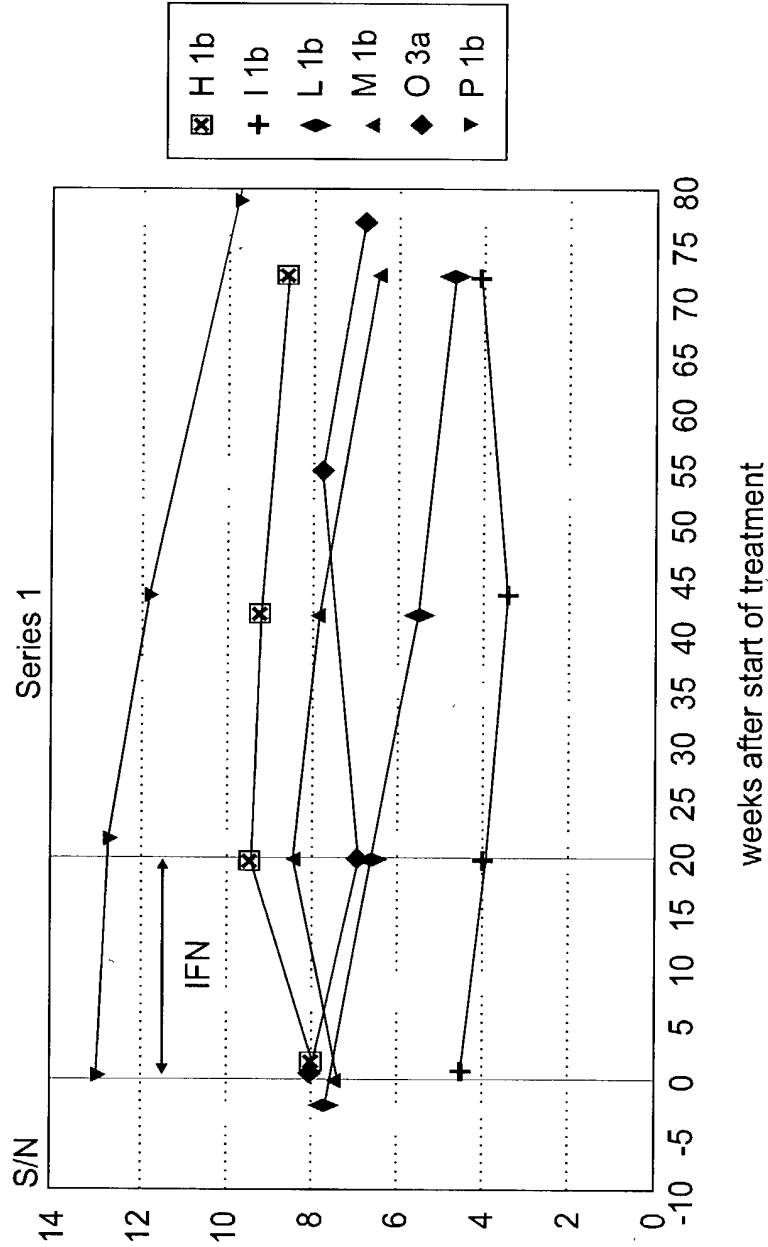


Figure 10



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 11 of 64  
Atty. Dkt.: 2551-69

# Anti-E2 levels in INCOMPLETE responders to IFN treatment

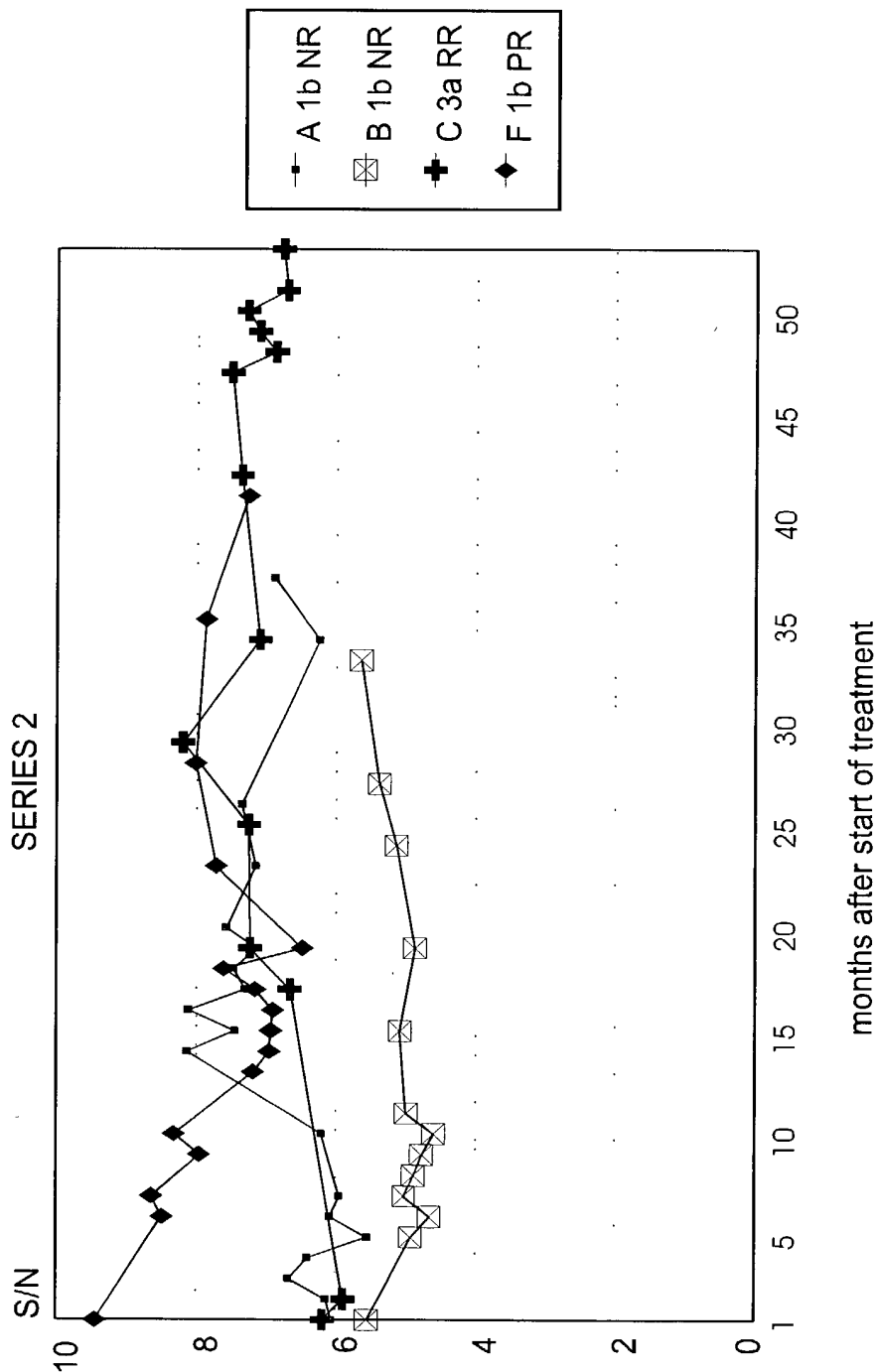


Figure 11



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 12 of 64  
Atty. Dkt.: 2551-69

# Anti-E2 levels in COMPLETE responders to IFN treatment

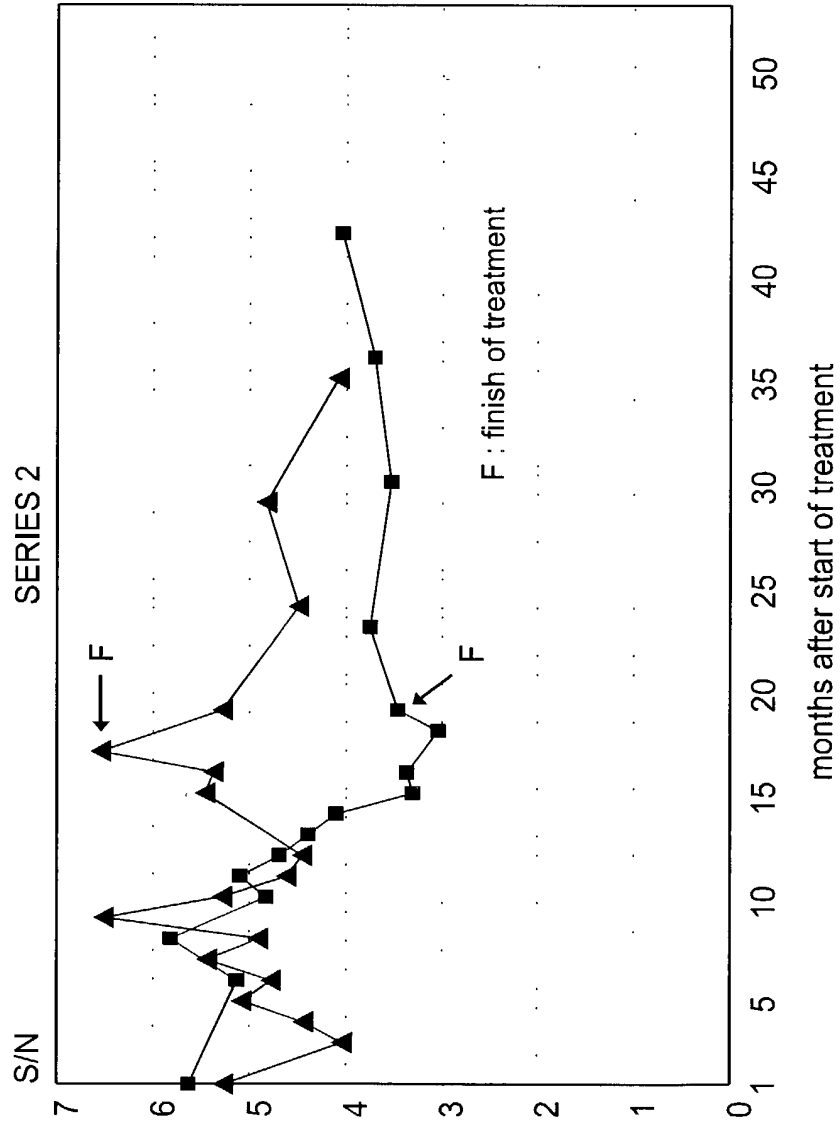


Figure 12

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 13 of 64  
Atty. Dkt.: 2551-69



# Human anti-E1 reactivity competed with peptides

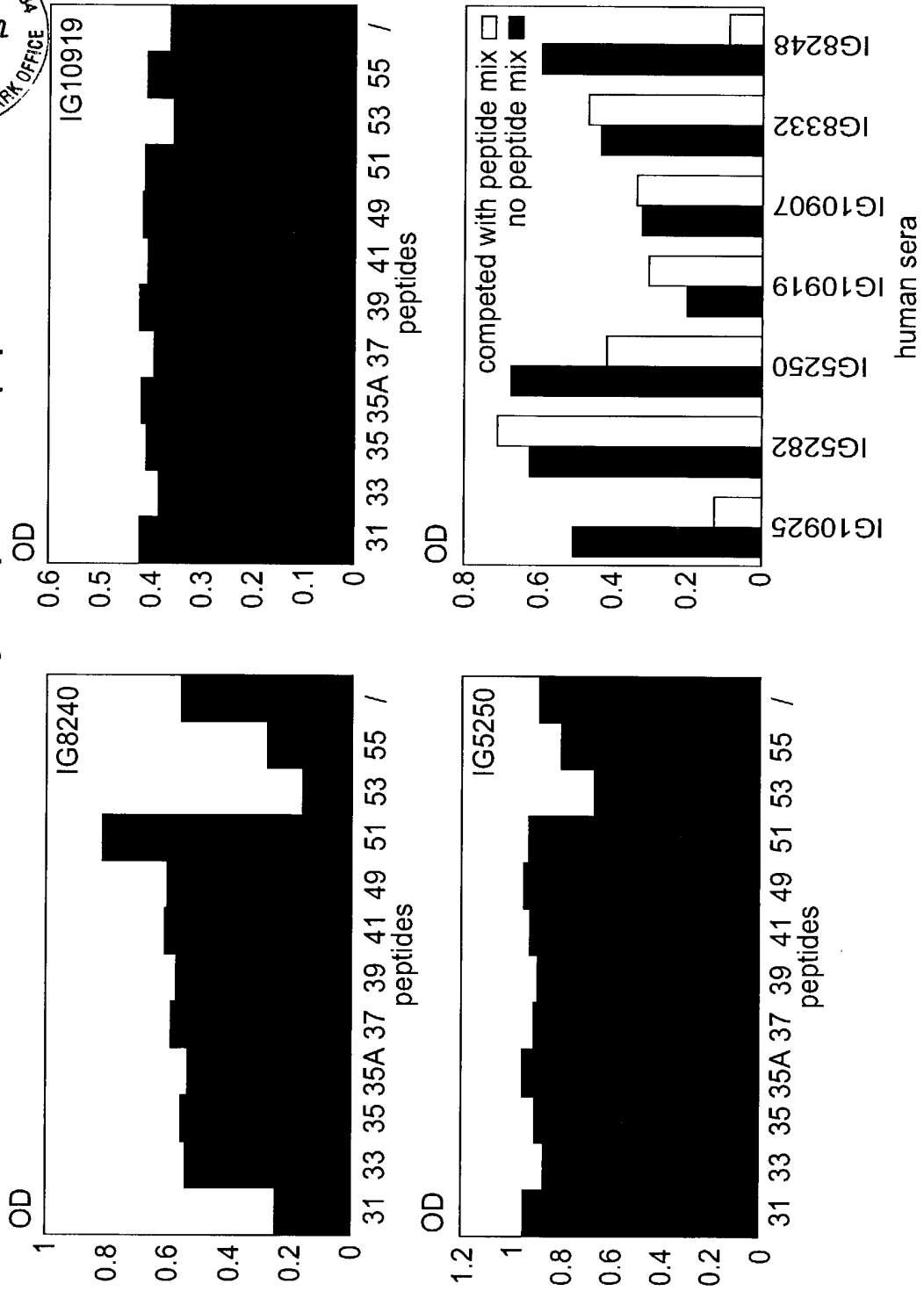


Figure 13



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 14 of 64  
Atty. Dkt.: 2551-69

# Competition of reactivity of anti-E1 Mabs with peptides

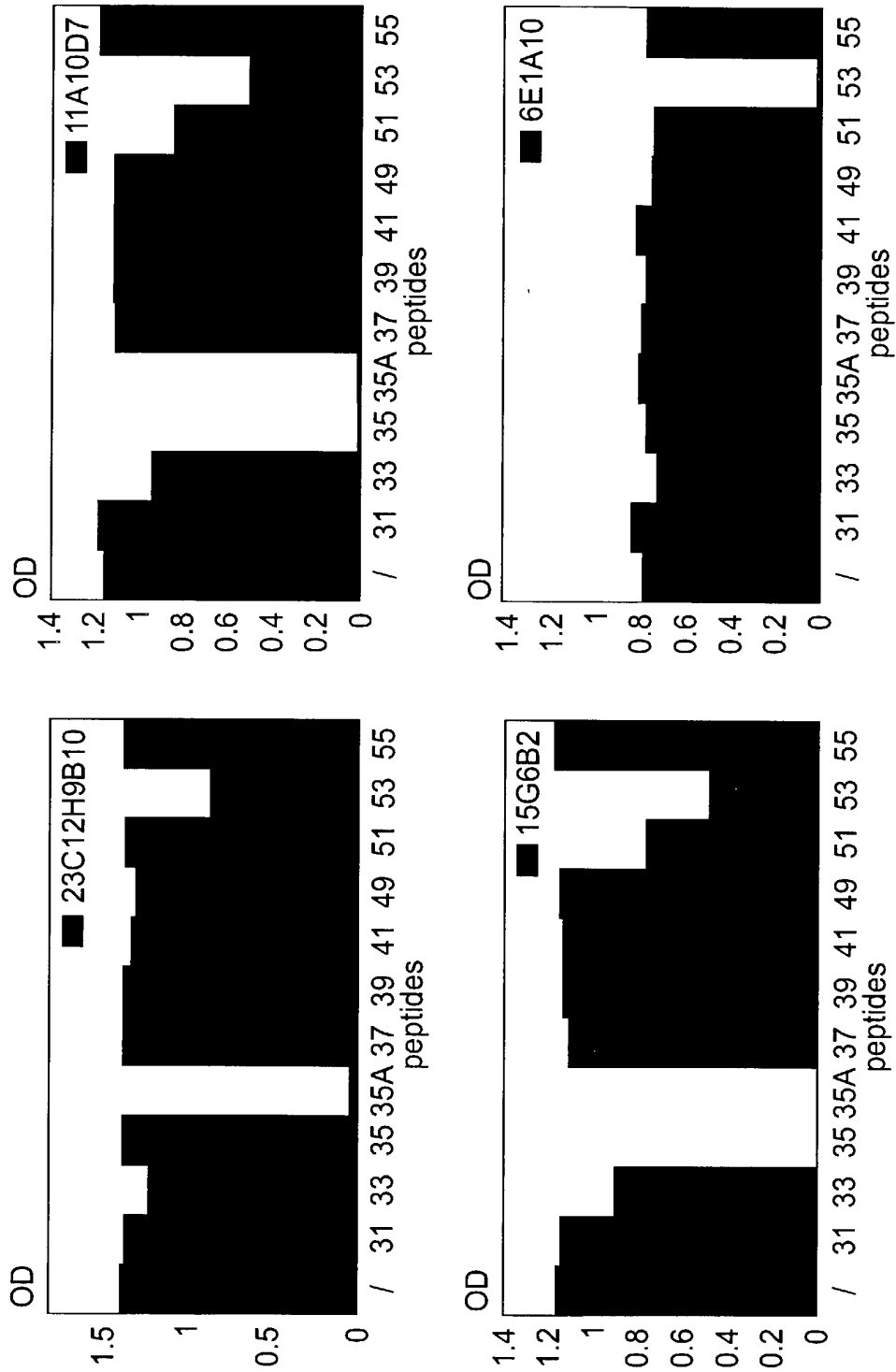


Figure 14



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 15 of 64  
Atty. Dkt.: 2551-69

# Anti-E1 (epitope 1) levels in NON-RESPONDERS to IFN treatment

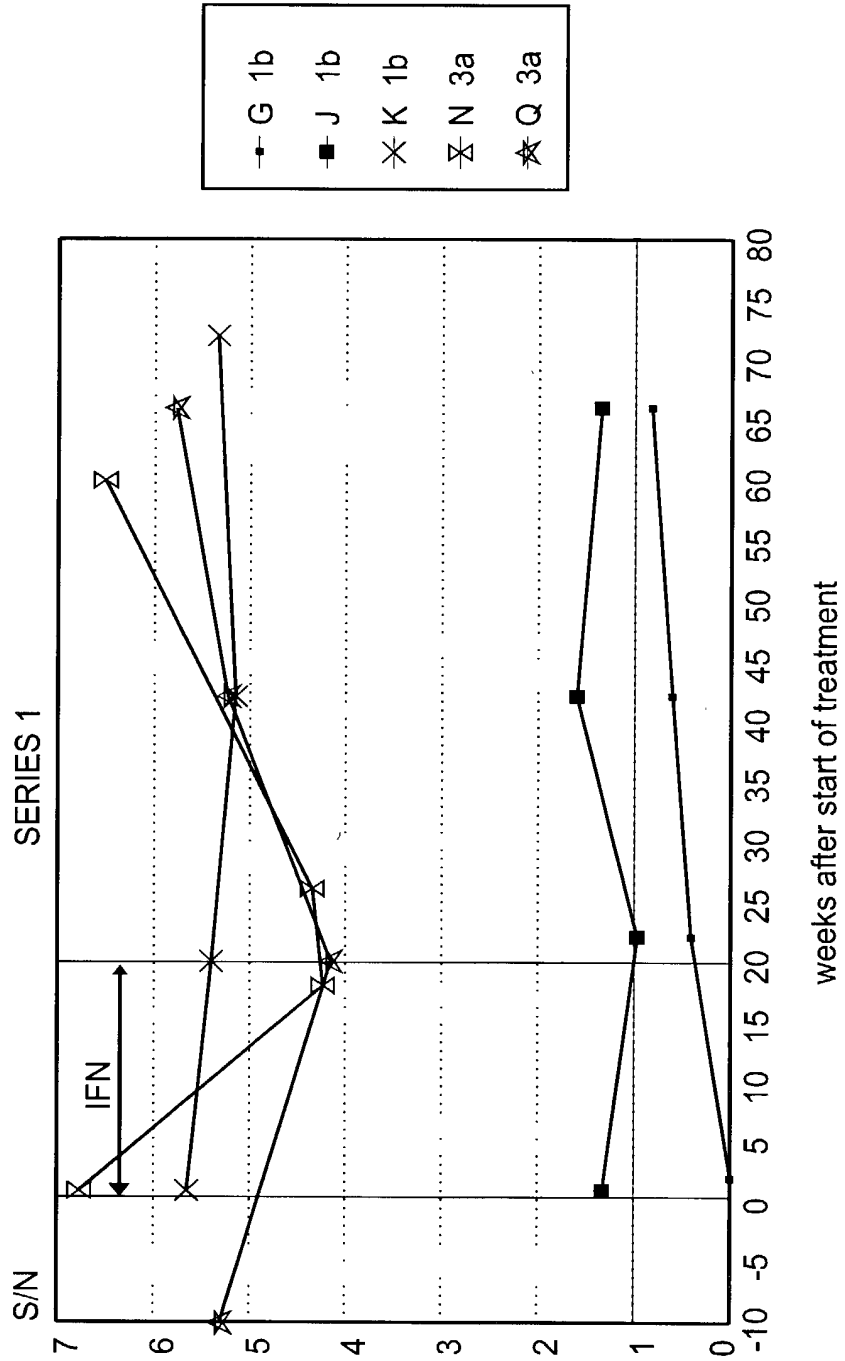


Figure 15



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 16 of 64  
Atty. Dkt.: 2551-69

# Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment

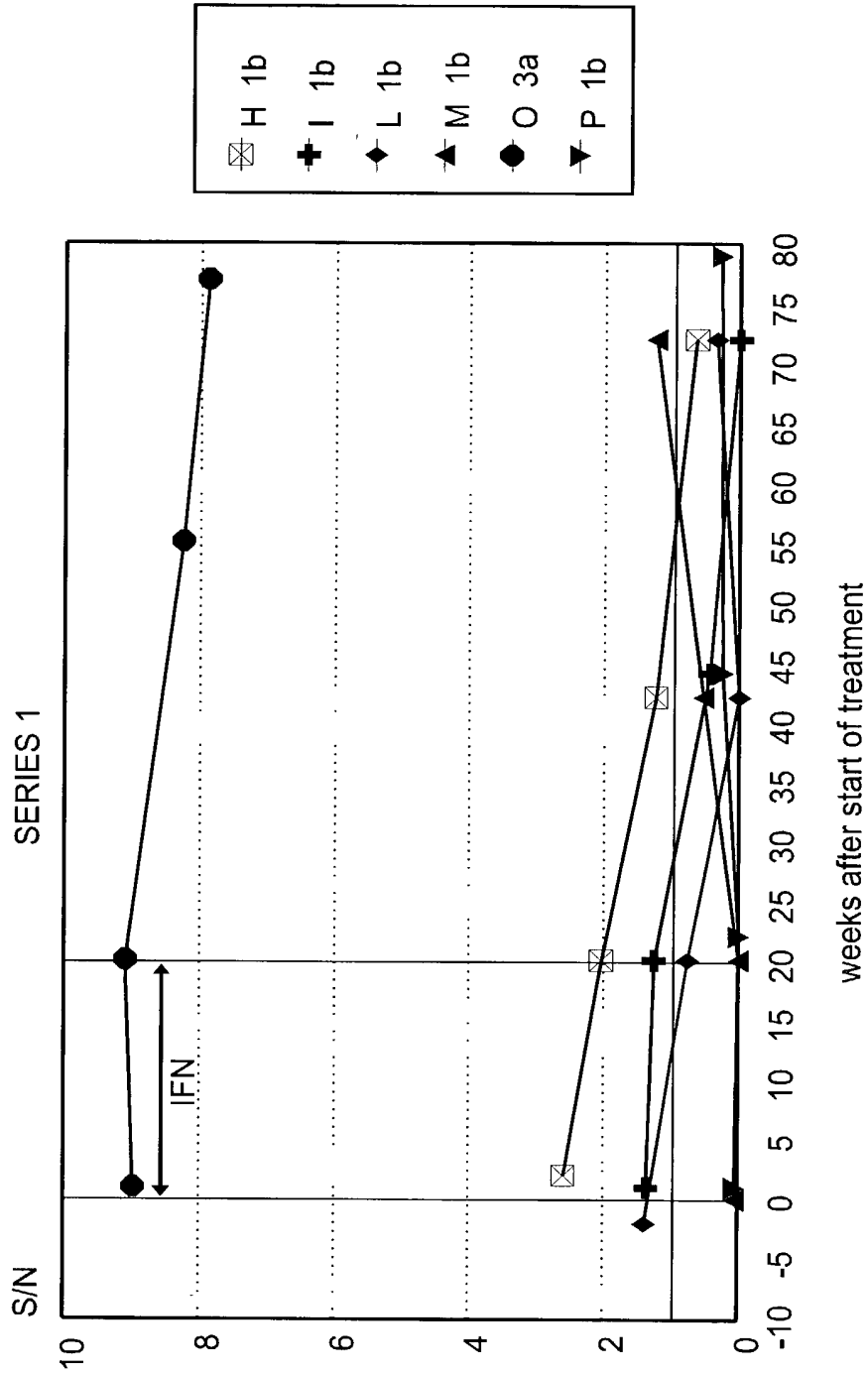


Figure 16





Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 17 of 64  
Atty. Dkt.: 2551-69

# Anti-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment

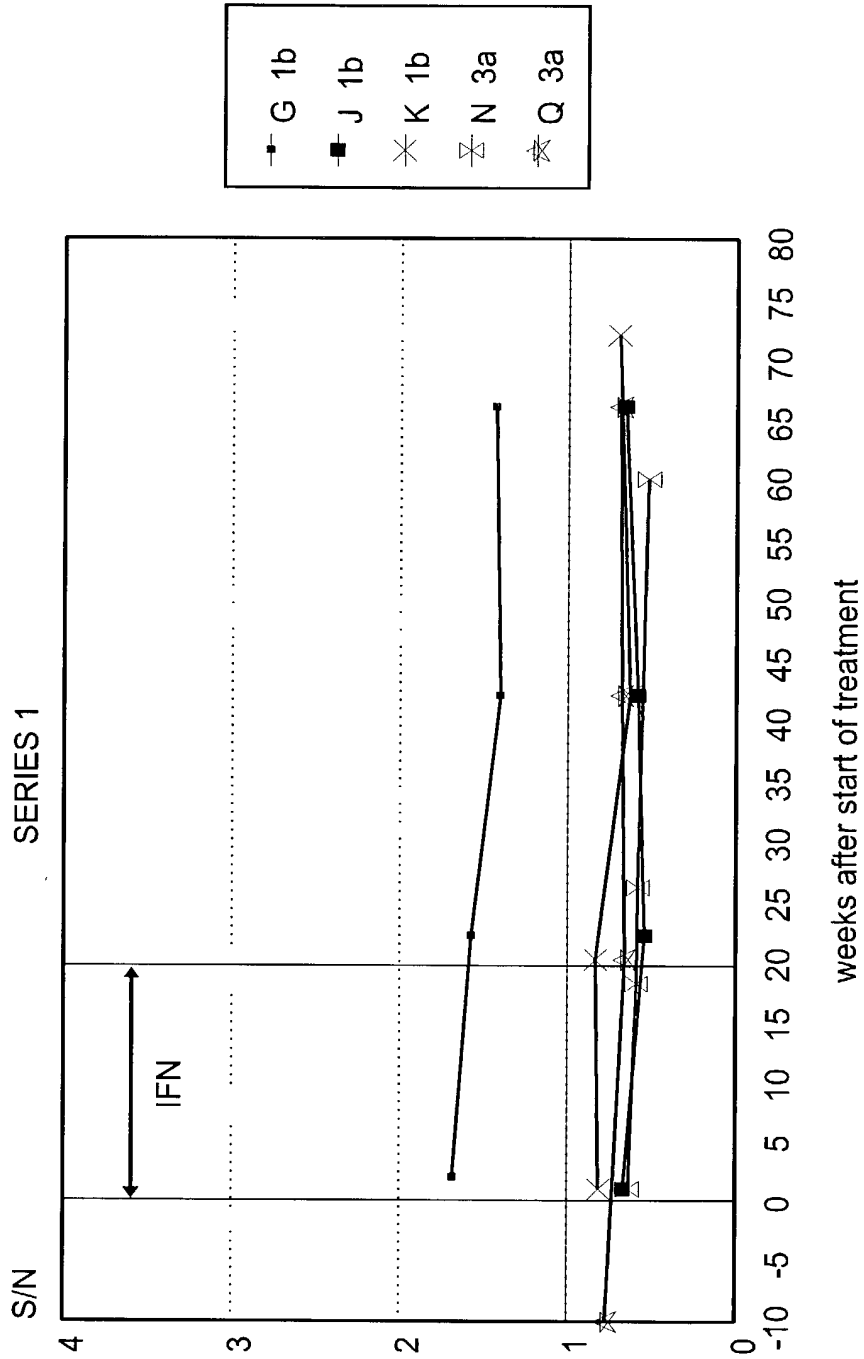


Figure 17

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 18 of 64  
Atty. Dkt.: 2551-69



# Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

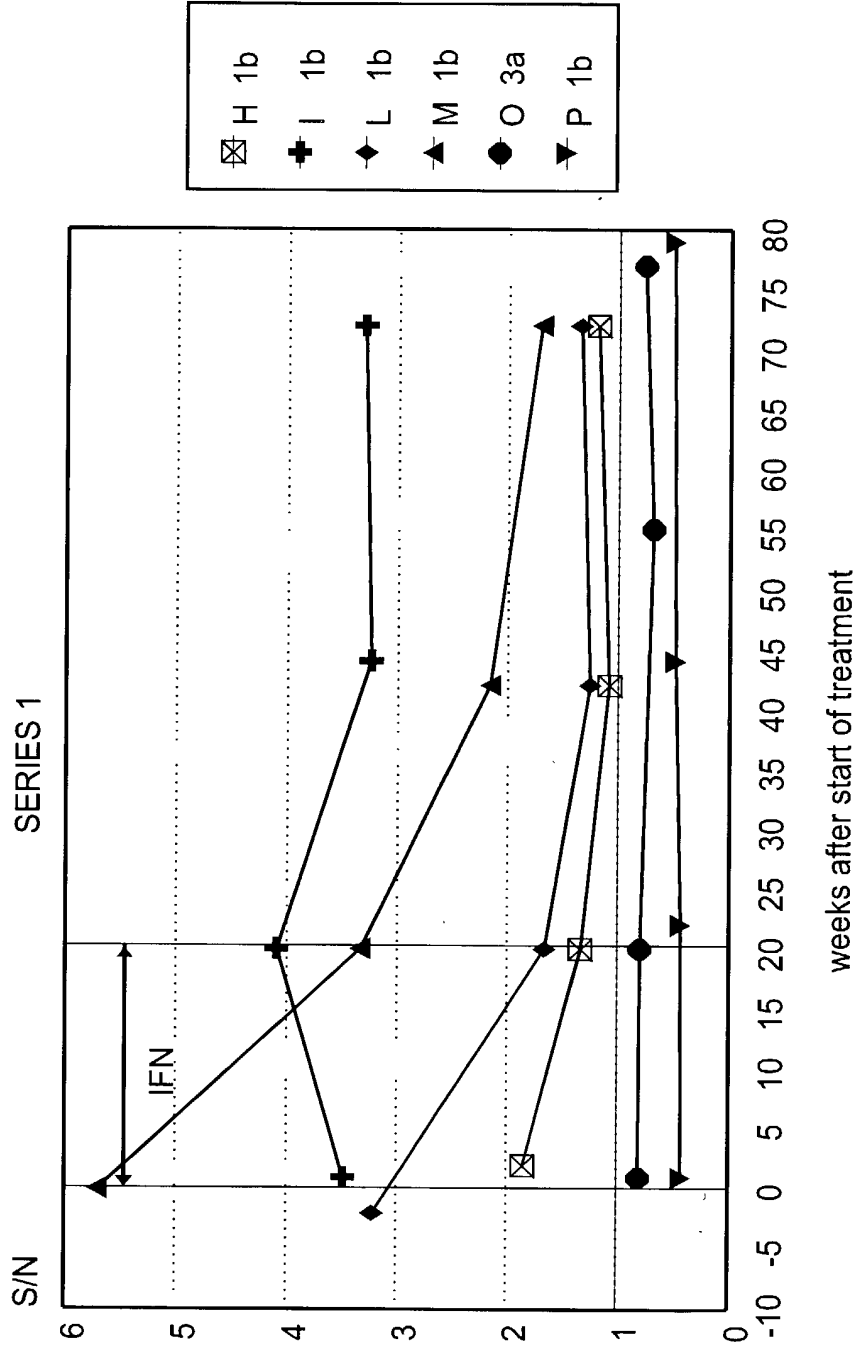


Figure 18

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 19 of 64  
Atty. Dkt.: 2551-69



# Competition of reactivity of anti-E2 Mabs with peptides

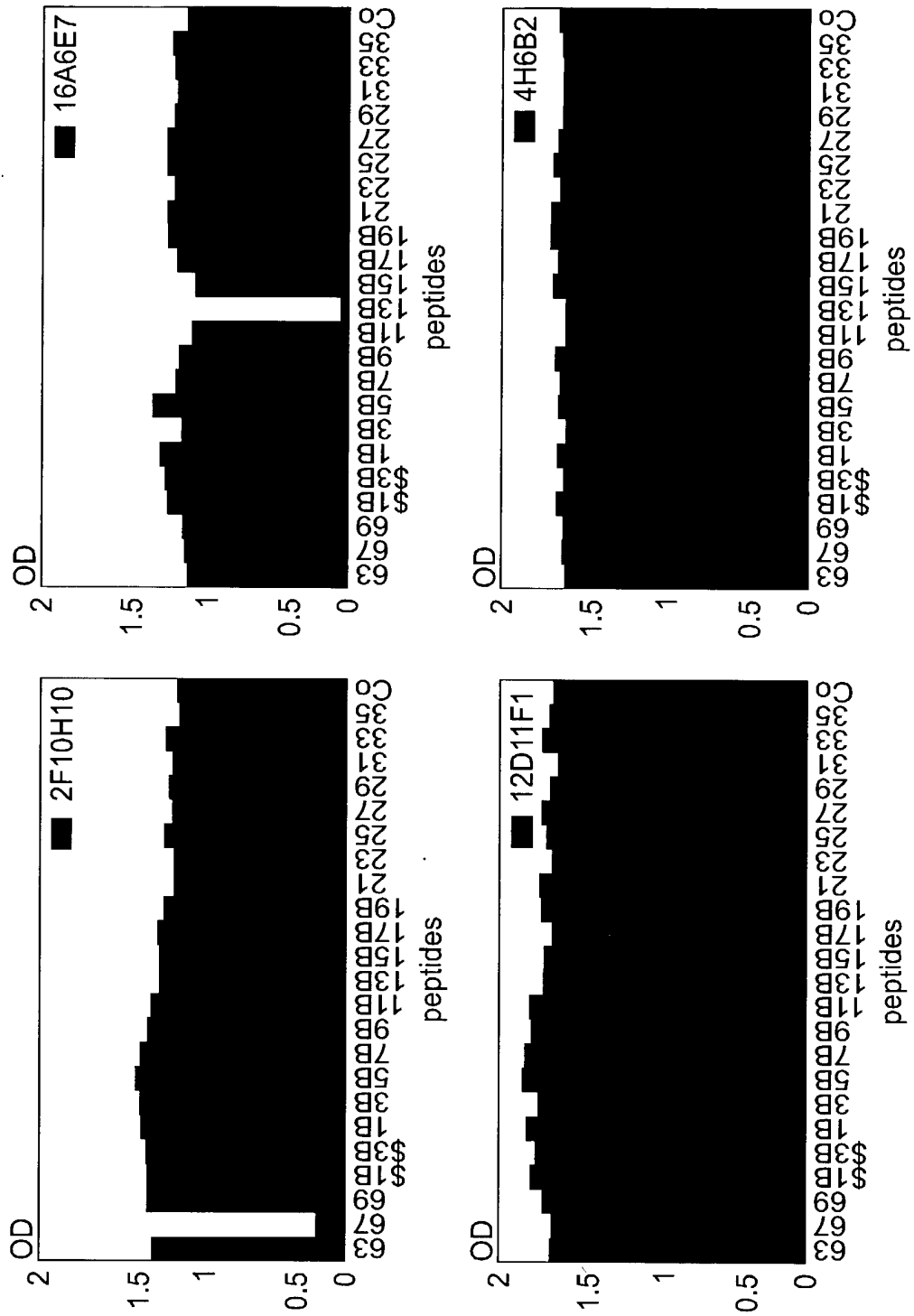


Figure 19

## Human anti-E2 reactivity competed with peptides

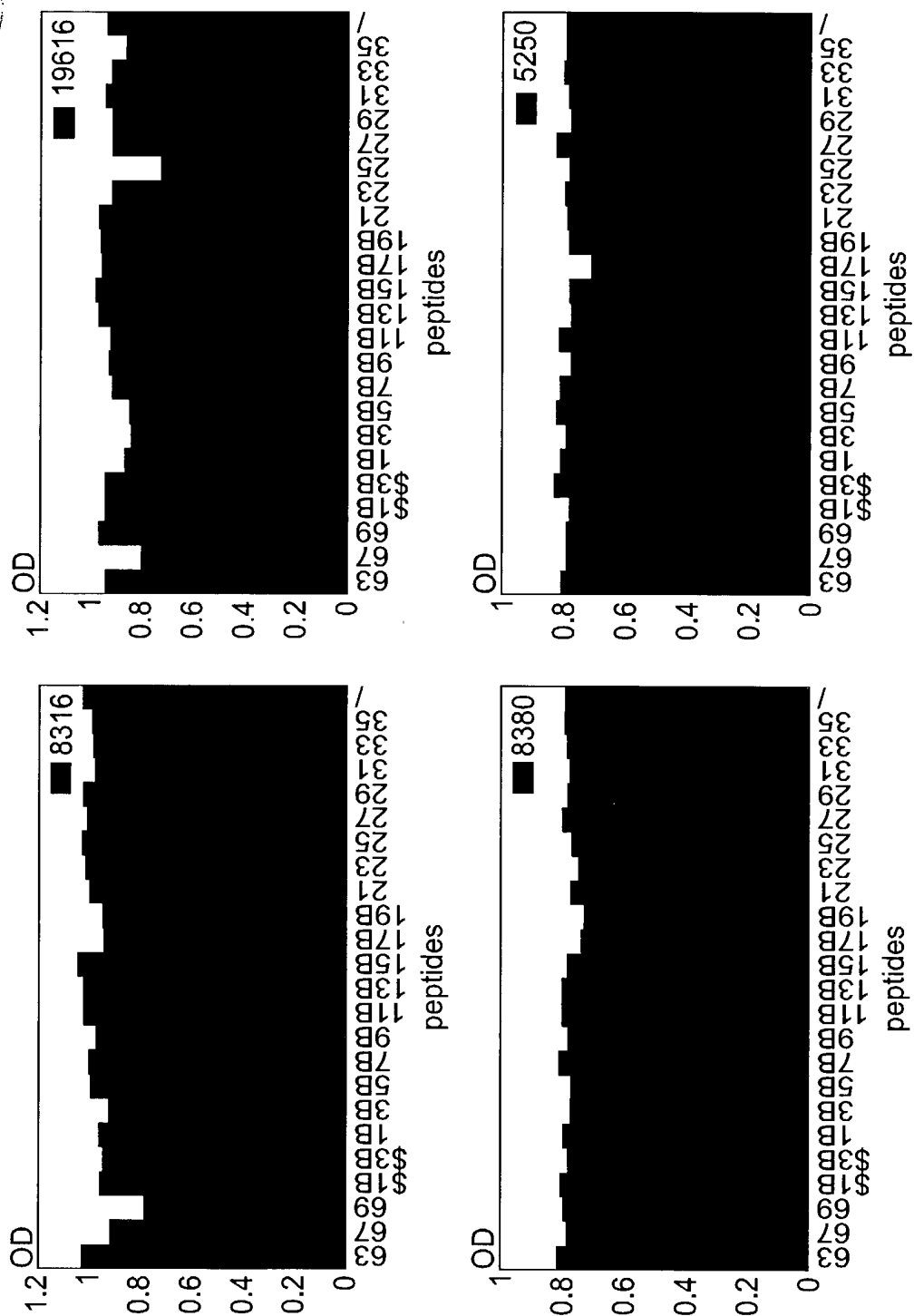


Figure 20



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 21 of 64  
 Atty. Dkt.: 2551-69

GGCATGCAAGCTTAATTAATT 3' (SEQ ID NO 1)  
 3'ACGTCCGTACGTTTCAATTAATTAATCGA 5' (SEQ ID NO 94)

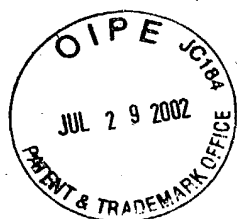
5'CCGGGGAGGCCTGCACGTGATCGAGGGCAGACACCATCACCACCATCACTAATAGTTA  
 ATTAAGTCA 3' (SEQ ID NO 2)  
 3'CCTCCGGACGTGCACTAGCTCCCGTCTGTGGTAGTGGTGGTAGTGATTATCAATTAAT  
 TG 5' (SEQ ID NO 95)

SEQ ID NO 3 (HCC19A)  
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 GCTTCCGCTTATGAGGTGCGCAACGTGTCCGGGATGTACCATGTCACGAACGACTGCTCC  
 AACTCAAGCATTGTGTATGAGGCAGCGGACATGATGCACACCCCCGGGTGCGTGCCC  
 TGGCTTCCGGGAGAACAACCTTTCCCGCTGCTGGGTAGCGCTCACCCCCACGCTCGCAGCT  
 AGGAACGCCAGCGTCCCCACCACGACAATACGACGCCACGTGATTTGCTCGTTGGGGCG  
 GCTGCTCTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTCTTCTCTGCTCTCC  
 CAGCTGTTCAACCATCTCGCCTCGCCGGCATGAGACGGTGCAGGACTGCAATTGCTCAATC  
 TATCCCGGCCACATAACAGGTCAACGTATGGCTTGGGATATGATGATGAAGTGGTGCCT  
 ACAACGGCCCTGGTGGTATCGCAGCTGCTCCGGATCCCAAGCTGTCGTGGACATGGTG  
 GCGGGGGCCCATTTGGGGAGTCTTGGCGGGCCTCGCCTACTATTCCATGGTGGGGAAGTGG  
 GCTAAGGTTTTGATTGTGATGCTACTCTTTGCTCTCTAATAG

SEQ ID NO 5 (HCC110A)  
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 TGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACCACGACA  
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 GGGGACCTCTGCGGATCTGTCTTCTCTGCTCTCCAGCTGTTCAACCATCTCGCCTCGCCGG  
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 ATGGCTTGGGATATGATGATGAAGTGGTGCCTACAACGGCCCTGGTGGTATCGCAGCTG  
 CTCCGGATCCCAAGCTGTGCTGGACATGGTGGCGGGGGCCCATTTGGGGAGTCTTGGCG  
 GGTCTCGCCTACTATTCCATGGTGGGGAAGTGGGCTAAGGTTTTGATTGTGATGCTACTC  
 TTTGCTCCCTAATAG

SEQ ID NO 7 (HCC111A)

Figure 21A



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 22 of 64  
 Atty. Dkt.: 2551-69

ATGTTGGGTAAGGTCATCGATACCCTTACGTGCGGCTTCGCCGACCTCATGGGGTACATT  
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 CTCTTGGCTTTACTGTCTGTCTGACCATTCCAGCTTCCGCTTATGAGGTGCGCAACGTG  
 TCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATGAGGCAGCG  
 GACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAACAACCTTTCCCGC  
 TGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACTACGACA  
 ATACGACGCCACGTGCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTTCCGCTATGTACGTG  
 GGGGATCTCTGCGGATCTGTCTTCTCGTCTCCAGCTGTTACCATCTCGCCTCGCCGG  
 CATGAGACGGTGCAAGACTGCAATTGCTCAATCTATCCCGGCCACATAACAGGTCACCGT  
 ATGGCTTGGGATATGATGATGAACTGGTAATAG

SEQ ID NO 9 (HCC112A)

ATGCCCCGTTGCTCTTTCTCTATCTTCTTGGCCCTGCTGTCTGTCTGACCATACCA  
 GCTTCCGCTTATGAAGTGCGCAACGTGTCCGGGGTGTAACATGTACGAACGACTGCTCC  
 AACTCAAGCATAGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCC  
 TGCGTTCCGGAGGGCAACTCCTCCCGTTGCTGGGTGGCGCTCACTCCCACGCTCGCGGCC  
 AGGAACGCCAGCGTCCCCACAACGACAATACGACGCCACGTGCGATTTGCTCGTTGGGGCT  
 GCTGCTTTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCTTGTTC  
 CAGCTGTTACCTTCTCACCTCGCCGGCATCAAACAGTACAGGACTGCAACTGCTCAATC  
 TATCCCGGCCATGTATCAGGTCACCGCATGGCTTGGGATATGATGATGAACTGGTCCTAA  
 TAG

SEQ ID NO 11 (HCC113A)

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 GCTTCCGCTTATGAAGTGCGCAACGTGTCCGGGGTGTAACATGTACGAACGACTGCTCC  
 AACTCAAGCATAGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGGTGCGTGCCC  
 TGCGTTCCGGAGGGCAACTCCTCCCGTTGCTGGGTGGCGCTCACTCCCACGCTCGCGGCC  
 AGGAACGCCAGCGTCCCCACAACGACAATACGACGCCACGTGCGATTTGCTCGTTGGGGCT  
 GCTGCTTTCTGTTCCGCTATGTACGTGGGGGATCTCTGCGGATCTGTTTTCTTGTTC  
 CAGCTGTTACCTTCTCACCTCGCCGGCATCAAACAGTACAGGACTGCAACTGCTCAATC  
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SEQ ID NO 13 (HCC117A)

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 CTCTTGGCTTTACTGTCTGTCTAACCATTCCAGCTTCCGCTTACGAGGTGCGCAACGTG  
 TCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATGAGGCAGCG  
 GACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAACAACCTTTCCCGC  
 TGCTGGGTAGCGCTCACCCCCACGCTCGCGGCTAGGAACGCCAGCATCCCCACTACAACA

Figure 21B



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 23 of 64  
 Atty. Dkt.: 2551-69

ATACGACGCCACGTCGATTTGCTCGTTGGGGCGGCTGCTTTCTGTTCCGCTATGTACGTG  
 GGGGATCTCTGCGGATCTGTCTTCCTCGTCTCCCAGCTGTTACCATCTCGCCTCGCCGG  
 CATGAGACGGTGACGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTCACCGT  
 ATGGCTTGGGATATGATGATGAACTGGTACTAATAG

SEQ ID NO 15 (HCP<sub>r</sub>51)

ATGCCCCGTTGCTCTTTCTCTATCTT

SEQ ID NO 16 (HCP<sub>r</sub>52)

ATGTTGGGTAAGGTCATCGATACCCCT

SEQ ID NO 17 (HCP<sub>r</sub>53)

CTATTAGGACCAGTTCATCATCATATCCCA

SEQ ID NO 18 (HCP<sub>r</sub>54)

CTATTACCAGTTCATCATCATATCCCA

SEQ ID NO 19 (HCP<sub>r</sub>107)

ATACGACGCCACGTCGATTTCCAGCTGTTACCATC

SEQ ID NO 20 (HCP<sub>r</sub>108)

GATGGTGAACAGCTGGGAATCGACGTGGCGTCGTAT

SEQ ID NO 21 (HCC137)

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 CTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCGCAACGTG  
 TCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATGAGGCAGCG  
 GACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAACAACTCTTCCCGC  
 TGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACCACGACA  
 ATACGACGCCACGTCGATTTCCAGCTGTTACCATCTCGCCTCGCCGGCATGAGACGGTG  
 CAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTCACCGTATGGCTTGGGAT  
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 CAAGCTGTCTGGACATGGTGGCGGGGGGCCATTGGGGAGTCTGGCGGGTCTCGCCTAC  
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 TAG

SEQ ID NO 23 (HCC138)

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 CTGGAGGACGGCGTGAACATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCTATCTTC  
 CTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCGCAACGTG  
 TCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATGAGGCAGCG

Figure 21C



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 24 of 64  
Atty. Dkt.: 2551-69

GACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCTGGGAGAACAACCTCTTCCCGC  
TGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACCACGACA  
ATACGACGCCACGTCGATTCCCAGCTGTTACCATCTCGCCTCGCCGGCATGAGACGGTG  
CAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTACCGTATGGCTTGGGAT  
ATGATGATGAACTGGTAATAG

SEQ ID NO 25 (HCC139)

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CCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCGGGTT  
CTGGAGGACGGCGTGAACATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCTATCTTC  
CTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCGCAACGTG  
TCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATGAGGCAGCG  
GACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCTGGGAGAACAACCTCTTCCCGC  
TGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACCACGACA  
ATACGACGCCACGTCGATTCCCAGCTGTTACCATCTCGCCTCGCCGGCATGAGACGGTG  
CAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTACCGTATGGCTTGGGAT  
ATGATGATGAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTGCTCCGGATCCTC  
TAATAG

SEQ ID NO 27 (HCC140)

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CCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCGGGTT  
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CTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCGCAACGTG  
TCCGGGATGTACCATGTACGAACGACTGCTCCAACCTCAAGCATTGTGTATGAGGCAGCG  
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ATACGACGCCACGTCGATTCCCAGCTGTTACCATCTCGCCTCGCCGGCATGAGACGGTG  
CAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTACCGTATGGCTTGGGAT  
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ATCGAGGGCAGACACCATCACCACCATCACTAATAG

SEQ ID NO 29 (HCC162)

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GAAGACGGGATAAATTTGCAACAGGGAATTTGCCCGGTTGCTCCTTTTCTATTTTCCTT  
CTCGCTCTGTTCTTGTCTAATTCATCCAGCAGCTAGTCTAGAGTGCGGGAATACGTCT  
GGCCTCTATGTCCTTACCAACGACTGTTCCAATAGCAGTATTGTGTACGAGGCCGATGAC  
GTTATTCTGCACACACCCGGCTGCATACCTTGTGTCCAGGACGGCAATACATCCACGTGC  
TGGACCCAGTGACACCTACAGTGGCAGTCAAGTACGTGCGAGCAACCACCGCTTCGATA  
CGCAGTCATGTGGACCTATTAGTGGGCGCGGCCACGATGTGCTCTGCGCTCTACGTGGGT  
GACATGTGTGGGGCTGTCTTCTCGTGGGACAAGCCTTCACGTTACAGACCTCGTCGCCAT

Figure 21D





Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 25 of 64  
Atty. Dkt.: 2551-69

CAAACGGTCCAGACCTGTAACTGCTCGCTGTACCCAGGCCATCTTTCAGGACATCGAATG  
GCTTGGGATATGATGATGAACTGGTAATAG

SEQ ID NO 31 (HCC163)

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CTCGTAGGCGGGCCCATTTGGGGGCGTCGCAAGGGCTCTCGCACACGGTGTGAGGGTCCTT  
GAGGACGGGGTAAACTATGCAACAGGGAATTTACCCGGTTGCTCTTTCTCTATCTTTATT  
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GGGATTTATCATGTTACCAATGATTGCCCAAACCTCTTCATAGTCTATGAGGCAGATAAC  
CTGATCCTACACGCACCTGGTTGCGTGCCCTGTGTCTGACAGGTAATGTGAGTAGATGC  
TGGGTCCAAATTACCCCTACACTGTCAGCCCCGAGCCTCGGAGCAGTCACGGCTCCTCTT  
CGGAGAGCCGTTGACTACCTAGCGGGAGGGGCTGCCCTCTGCTCCGCGTTATACGTAGGA  
GACGCGTGTGGGGCACTATTCTTGGTAGGCCAAATGTTACCTATAGGCCTCGCCAGCAC  
GCTACGGTGCAGAACTGCAACTGTTCCATTTACAGTGGCCATGTTACCGGCCACCGGATG  
GCATGGGATATGATGATGAACTGGTAATAG

SEQ ID NO 33 (HCP109)

TGGGATATGATGATGAACTGGTC

SEQ ID NO 34 (HCP172)

CTATTATGGTGGTAAKGCCARCARGAGCAGGAG

SEQ ID NO 35 (HCCL22A)

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GCCTACTATTCCATGGTGGGGAACCTGGGCTAAGGTTTTGGTTGTGATGCTACTCTTTGCC  
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GCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAGCGCTTGGCCAGCTGT  
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GGGCCCTGGCTGACACCTAGGTGTATGGTTCATTACCCATATAGGCTCTGGCACTACCCC  
TGCACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGCACAGG  
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TCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGATACTGCCCTGTTCTTCTC

Figure 21E

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 26 of 64  
 Atty. Dkt.: 2551-69



ACCACCCTGCCGGCCCTATCCACCGGCCTGATCCACCTCCATCAGAACATCGTGGACGTG  
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 CTGATAGCTCAAGCTGAGGCCGCCTTAGAGAACCTGGTGGTCCTCAATGCGGCGGCCGTG  
 GCCGGGGCGCATGGCACTCTTTCCTTCCTTGTGTTCTTCTGTGCTGCCTGGTACATCAAG  
 GGCAGGCTGGTCCCTGGTGCGGCATACGCCTTCTATGGCGTGTGGCCGCTGCTCCTGCTT  
 CTGCTGGCCTTACCACCACGAGCTTATGCCTAGTAA

SEQ ID NO 37 (HCC141)

GATCCCAACAAGCTGTCGTGGACATGGTGGCGGGGGGCCATTGGGGAGTCCTGGCGGGCCT  
 CGCCTACTATTCCATGGTGGGGAAGTGGGCTAAGGTTTTGGTTGTGATGCTACTCTTTGC  
 CGGCGTCGACGGGCATACCCGCGTGTGAGGAGGGGCAGCAGCCTCCGATACCAGGGGCCT  
 TGTGTCCCTCTTTAGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAG  
 TTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGC  
 CGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAGCGCTTGGCCAGCTG  
 TCGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTTACACTGAGCCTAACAG  
 CTCGGACCAGAGGGCCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCGC  
 GTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGACGAC  
 CGATCGGTTTTGGTGTCCCCACGTATAACTGGGGGGCGAACGACTCGGATGTGCTGATTCT  
 CAACAACACGCGGCCGCGCGAGGCAACTGGTTCGGCTGTACATGGATGAATGGCACTGG  
 GTTCACCAAGACGTGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTT  
 GACCTGCCCCACTGACTGTTTTCGGAAGCACCCCGAGGCCACCTACGCCAGATGCGGTTCT  
 TGGGCCCTGGCTGACACCTAGGTGTATGGTTTATTACCCATATAGGCTCTGGCACTACCC  
 CTGCACTGTCAACTTCACCATCTTCAAGTTAGGATGTACGTGGGGGGCGTGGAGCACAG  
 GTTCGAAGCCGCATGCAATTGGAAGTGTGAGGAGAGCGTTGTGACTTGGAGGACAGGGATAG  
 ATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGAGTGGCAGAGCTTAATT  
 AATTAG

SEQ ID NO 39 (HCC142)

GATCCCAACAAGCTGTCGTGGACATGGTGGCGGGGGGCCATTGGGGAGTCCTGGCGGGCCT  
 CGCCTACTATTCCATGGTGGGGAAGTGGGCTAAGGTTTTGGTTGTGATGCTACTCTTTGC  
 CGGCGTCGACGGGCATACCCGCGTGTGAGGAGGGGCAGCAGCCTCCGATACCAGGGGCCT  
 TGTGTCCCTCTTTAGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAG  
 TTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGC  
 CGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAGCGCTTGGCCAGCTG  
 TCGCTCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTTACACTGAGCCTAACAG  
 CTCGGACCAGAGGGCCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCGC  
 GTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGACGAC  
 CGATCGGTTTTGGTGTCCCCACGTATAACTGGGGGGCGAACGACTCGGATGTGCTGATTCT  
 CAACAACACGCGGCCGCGCGAGGCAACTGGTTCGGCTGTACATGGATGAATGGCACTGG  
 GTTCACCAAGACGTGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTT

Figure 21F



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 27 of 64  
 Atty. Dkt.: 2551-69

GACCTGCCCCACTGACTGTTTTCGGAAGCACCCCGAGGCCACCTACGCCAGATGCGGTTTC  
 TGGGCCCTGGCTGACACCTAGGTGTATGGTTCATTACCCATATAGGCTCTGGCACTACCC  
 CTGCACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGCACAG  
 GTTCGAAGCCGCATGCAATTGGACTCGAGGAGAGCGTTGTGACTTGGAGGACAGGGATAG  
 ATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGGTGATCGAGGGCAGACACCATCACC  
 ACCATCACTAATAG

SEQ ID NO 41 (HCC143)

ATGGTGGGGAAGTGGGCTAAGGTTTTGGTTGTGATGCTACTCTTTGCCGGCGTTCGACGGG  
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 AGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCACATCAAC  
 AGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCACTATTCTAC  
 AAACACAAATTCAACTCGTCTGGATGCCCAGAGCGCTTGGCCAGCTGTGCTCCATCGAC  
 AAGTTCGCTCAGGGGTGGGGTCCCCCTCACTTACACTGAGCCTAACAGCTCGGACCAGAGG  
 CCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCGCGTCTCAGGTGTGC  
 GGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGACGACCGATCGGTTTGGT  
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 CCGCCGCGAGGCAACTGGTTCCGCTGTACATGGATGAATGGCACTGGGTTTACCAAGACG  
 TGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACT  
 GACTGTTTTTCGGAAGCACCCCGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTG  
 ACACCTAGGTGTATGGTTCATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAAC  
 TTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGCACAGGTTTGAAGCCGCA  
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 CCGCTGCTGCTGTCTACAACAGAGTGGCAGAGCTTAATTAATTAG

SEQ ID NO 43 (HCC144)

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 AGCCCCGGGTGCGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCACATCAAC  
 AGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCACTATTCTAC  
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 CCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCGCGTCTCAGGTGTGC  
 GGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGGGACGACCGATCGGTTTGGT  
 GTCCCCACGTATAACTGGGGGGCGAACGACTCGGATGTGCTGATTCTCAACAACACGCGG  
 CCGCCGCGAGGCAACTGGTTCCGCTGTACATGGATGAATGGCACTGGGTTTACCAAGACG  
 TGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACT  
 GACTGTTTTTCGGAAGCACCCCGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTG  
 ACACCTAGGTGTATGGTTCATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAAC  
 TTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGCACAGGTTTGAAGCCGCA  
 TGCAATTGGACTCGAGGAGAGCGTTGTGACTTGGAGGACAGGGATAGATCAGAGCTTAGC

Figure 21G



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 28 of 64  
Atty. Dkt.: 2551-69

CCGCTGCTGCTGTCTACAACAGGTGATCGAGGGCAGACACCATCACCACCATCACTAATA

SEQ ID NO 45 (HCCL64)

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TCGGCTCAGAAAATCCAGCTCGTAAACACCAACGGCAGTTGGCACATCAACAGGACTGCC  
CTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCACTATTCTACAAACACAAA  
TTCAACTCGTCTGGATGCCAGAGCGCTTGGCCAGCTGTCGCTCCATCGACAAGTTCGCT  
CAGGGGTGGGGTCCCCTCACTTACACTGAGCCTAACAGCTCGGACCAGAGGCCCTACTGC  
TGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCGCGTCTCAGGTGTGCGGTCCAGTG  
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GGCAACTGGTTCGGCTGTACATGGATGAATGGCACTGGGTTCACCAAGACGTGTGGGGGC  
CCCCCGTGCAACATCGGGGGGGCCGGCAACAACACCTTGACCTGCCCCACTGACTGTTTT  
CGGAAGCACCCCGAGGCCACCTACGCCAGATGCGGTTCTGGGCCCTGGCTGACACCTAGG  
TGTATGGTTCATTACCCATATAGGCTCTGGCACTACCCCTGCACTGTCAACTTCACCATC  
TTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGCACAGGTTCTGAAGCCGCATGCAATTGG  
ACTCGAGGAGAGCGTTGTGACTTGGAGGACAGGGATAGATCAGAGCTTAGCCCGCTGCTG  
CTGTCTACAACAGAGTGGCAGATACTGCCCTGTTCTTACCACCCTGCCGGCCCTATCC  
ACCGGCCTGATCCACCTCCATCAGAACATCGTGGACGTGCAATACCTGTACGGTGTAGGG  
TCGGCGGTTGTCTCCCTTGTCTCAAAATGGGAGTATGTCCTGTTGCTCTTCTCTCTCTG  
GCAGACGCGCGCATCTGCGCCTGCTTATGGATGATGCTGCTGATAGCTCAAGCTGAGGCC  
GCCTTAGAGAACCTGGTGGTCTCAATGCGGCGGCCGTGGCCGGGGCGCATGGCACTCTT  
TCCTTCTTGTGTTCTTCTGTGCTGCCTGGTACATCAAGGGCAGGCTGGTCCCTGGTGGC  
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GCTTATGCCTAGTAA

SEQ ID NO 47 (HCC165)

AATTTGGGTAAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACATT  
CCGCTCGTCGGCGCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCGGGTT  
CTGGAGGACGGCGTGAACATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCTATCTTC  
CTCTTGGCTTTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCGCAACGTG  
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GACATGATCATGCACACCCCCGGGTGCGTGCCCTGCGTTCCGGGAGAACAACCTCTTCCCGC  
TGCTGGGTAGCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACCACGACA  
ATACGACGCCACGTGATTTGCTCGTTGGGGCGGCTGCTTTCTGTTCCGCTATGTACGTG  
GGGGACCTCTGCGGATCTGTCTTCTCGTCTCCAGCTGTTACCATCTCGCCTCGCCGG  
CATGAGACGGTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTACCCGT  
ATGGCTTGGGATATGATGATGAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTG  
CTCCGGATCCCACAAGCTGTGCTGGACATGGTGGCGGGGGCCCATTTGGGGAGTCCTGGCG

Figure 21H



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 29 of 64  
 Atty. Dkt.: 2551-69

GGCCTCGCCTACTATTCCATGGTGGGGAAGTGGGCTAAGGTTTTGGTTGTGATGCTACTC  
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 GGGCCTTGTGTCCCTCTTTAGCCCCGGGTGGGCTCAGAAAATCCAGCTCGTAAACACCAA  
 CGGCAGTTGGCACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTT  
 CTTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAGCGCTTGGC  
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 TAACAGCTCGGACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGT  
 ACCCGCGTCTCAGGTGTGCGGTCCAGTGTATTGCTTCACCCCGAGCCCTGTTGTGGTGGG  
 GACGACCGATCGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAACGACTCGGATGTGCT  
 GATTCTCAACAACACGCGGCCGCCGAGGCAACTGGTTCGGCTGTACATGGATGAATGG  
 CACTGGGTTCAACAAGACGTGTGGGGGGCCCCCGTGCAACATCGGGGGGGCCGGCAACAA  
 CACCTTGACCTGCCCCACTGACTGTTTTCGGAAGCACCCCGAGGCCACCTACGCCAGATG  
 CGGTTCTGGGCCCTGGCTGACACCTAGGTGTATGGTTCATTACCCATATAGGCTCTGGCA  
 CTACCCCTGCACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGA  
 GCACAGGTTGGAAGCCGCATGCAATTGGAAGTTCGAGGAGAGCGTTGTGACTTGGAGGACAG  
 GGATAGATCAGAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGATACTGCCCTG  
 TTCTTACACCACCTGCCGGCCCTATCCACCGGCCTGATCCACCTCCATCAGAACATCGT  
 GGACGTGCAATACCTGTACGGTGTAGGGTGGCGGTTGTCTCCCTTGTATCAAAATGGGA  
 GTATGTCTGTGCTCTTCTTCTCCTGGCAGACGCGCGCATCTGCGCCTGCTTATGGAT  
 GATGCTGCTGATAGCTCAAGCTGAGGCCGCTTAGAGAACCTGGTGGTCTCAATGCGGC  
 GGCGGTGGCCGGGGCGCATGGCACTCTTCTCTTCTTGTGTTCTTCTGTGCTGCCTGGTA  
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 CCTGCTTCTGCTGGCCTTACCACCACGAGCTTATGCCTAGTAAGCTT

SEQ ID NO 49 (HCC166)

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 GGCCCCAGGTTGGGTGTGCGCGGCACTAGGAAGACTTCCGAGCGGTGCAACCTCGTGGG  
 AGGCGACAACCTATCCCCAAGGCTCGCCGACCCGAGGGTAGGGCCTGGGCTCAGCCCGGG  
 TACCCTTGGCCCCCTCTATGGCAATGAGGGCATGGGGTGGGCAGGATGGCTCCTGTACCC  
 CGCGGCTCTCGGCCTAGTTGGGGCCCTACAGACCCCGGCGTAGGTGCGTAATTTGGGT  
 AAGGTCATCGATACCCTTACATGCGGCTTCGCCGACCTCGTGGGGTACATTCCGCTCGTC  
 GCGCCCCCCTAGGGGGCGCTGCCAGGGCCCTGGCGCATGGCGTCCGGGTTCTGGAGGAC  
 GCGGTGAACATATGCAACAGGGAATTTGCCCGGTTGCTCTTTCTCTATCTTCTCTTGGCT  
 TTGCTGTCTGTCTGACCGTTCCAGCTTCCGCTTATGAAGTGCGCAACGTGTCCGGGATG  
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 GCGCTCACCCCCACGCTCGCAGCTAGGAACGCCAGCGTCCCCACCACGACAATACGACGC  
 CACGTGATTTGCTCGTTGGGGCGGCTGCTTTCTGTTCCGCTATGTACGTGGGGGACCTC  
 TCGGATCTGTCTTCTCGTCTCCAGCTGTTACCATCTCGCCTCGCCGGCATGAGACG  
 GTGCAGGACTGCAATTGCTCAATCTATCCCGGCCACATAACGGGTACCGTATGGCTTGG

Figure 211



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 30 of 64  
Atty. Dkt.: 2551-69

ATATGATGATGAACTGGTCGCCTACAACGGCCCTGGTGGTATCGCAGCTGCTCCGGATC  
CCACAAGCTGTCGTGGACATGGTGGCGGGGGGCCATTGGGGAGTCCTGGCGGGCCTCGCC  
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GTCGACGGGCATACCCGCGTGTGAGGAGGGGAGCAGCCTCCGATACCAGGGGCTTGTG  
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CACATCAACAGGACTGCCCTGAACTGCAACGACTCCCTCCAAACAGGGTTCTTTGCCGCA  
CTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAGCGCTTGGCCAGCTGTGCG  
TCCATCGACAAGTTCGCTCAGGGGTGGGGTCCCCTCACTTACACTGAGCCTAACAGCTCG  
GACCAGAGGCCCTACTGCTGGCACTACGCGCCTCGACCGTGTGGTATTGTACCCGCGTCT  
CAGGTGTGCGGTCCAGTGTATTGCTTACCCCGAGCCCTGTTGTGGTGGGGACGACCGAT  
CGGTTTGGTGTCCCCACGTATAACTGGGGGGCGAACGACTCGGATGTGCTGATTCTCAAC  
AACACGCGGCCGCCGCGAGGCAACTGGTTCGGCTGTACATGGATGAATGGCACTGGGTTT  
ACCAAGACGTGTGGGGGCCCCCGTGCACATCGGGGGGGCCGGCAACAACACCTTGACC  
TGCCCCACTGACTGTTTTCGGAAGCACCCCGAGGCCACCTACGCCAGATGCGGTTCTGGG  
CCCTGGCTGACACCTAGGTGTATGGTTCATTACCCATATAGGCTCTGGCACTACCCCTGC  
ACTGTCAACTTCACCATCTTCAAGGTTAGGATGTACGTGGGGGGCGTGGAGCACAGGTTT  
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GAGCTTAGCCCGCTGCTGCTGTCTACAACAGAGTGGCAGATACTGCCCTGTTCTTACC  
ACCCTGCCGGCCCTATCCACCGGCCTGATCCACCTCCATCAGAACATCGTGGACGTGCAA  
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TTGCTCTTCTTCTCCTGGCAGACGCGCGCATCTGCGCCTGCTTATGGATGATGCTGCTG  
ATAGCTCAAGCTGAGGCCGCTTAGAGAACCTGGTGGTCTCAATGCGGCGGCCGTGGCC  
GGGGCGCATGGCACTCTTTCCTTCTTGTGTTCTTCTGTGCTGCCTGGTACATCAAGGGC  
AGGCTGGTCCCTGGTGCGGCATAACGCTTCTATGGCGTGTGGCCGCTGCTCCTGCTTCTG  
CTGGCCTTACCACCACGAGCTTATGCCTAGTAA

Figure 21J



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 31 of 64  
 Atty. Dkt.: 2551-69

OD measured at 450nm  
 construct

| Fraction     | Volume | dilution | 39<br>type 1b | 40<br>type 1b | 62<br>type 3a | 63<br>type 5a |
|--------------|--------|----------|---------------|---------------|---------------|---------------|
| Start        | 23ml   | 1/20     | 2.517         | 1.954         | 1.426         | 1.142         |
| Flow through | 23ml   | 1/20     | 0.087         | 0.085         | 0.176         | 0.120         |
| 1            | 0.4ml  | 1/200    | 0.102         | 0.051         | 0.048         | 0.050         |
| 2            |        |          | 0.396         | 0.550         | 0.090         | 0.067         |
| 3            |        |          | 2.627         | 2.603         | 2.481         | 2.372         |
| 4            |        |          | 3             | 2.967         | 3             | 2.694         |
| 5            |        |          | 3             | 2.810         | 2.640         | 2.154         |
| 6            |        |          | 2.694         | 2.499         | 1.359         | 1.561         |
| 7            |        |          | 2.408         | 2.481         | 0.347         | 1.390         |
| 8            |        |          | 2.176         | 1.970         | 1.624         | 0.865         |
| 9            |        |          | 1.461         | 1.422         | 0.887         | 0.604         |
| 10           |        |          | 1.286         | 0.926         | 0.543         | 0.519         |
| 11           |        |          | 0.981         | 0.781         | 0.294         | 0.294         |
| 12           |        |          | 0.812         | 0.650         | 0.249         | 0.199         |
| 13           |        |          | 0.373         | 0.432         | 0.239         | 0.209         |
| 14           |        |          | 0.653         | 0.371         | 0.145         | 0.184         |
| 15           |        |          | 0.441         | 0.348         | 0.151         | 0.151         |
| 16           |        |          | 0.321         | 0.374         | 0.098         | 0.106         |
| 17           |        |          | 0.525         | 0.186         | 0.099         | 0.108         |
| 18           |        |          | 0.351         | 0.171         | 0.083         | 0.090         |
| 19           |        |          | 0.192         | 0.164         | 0.084         | 0.087         |

Figure 22



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 32 of 64  
Atty. Dkt.: 2551-69

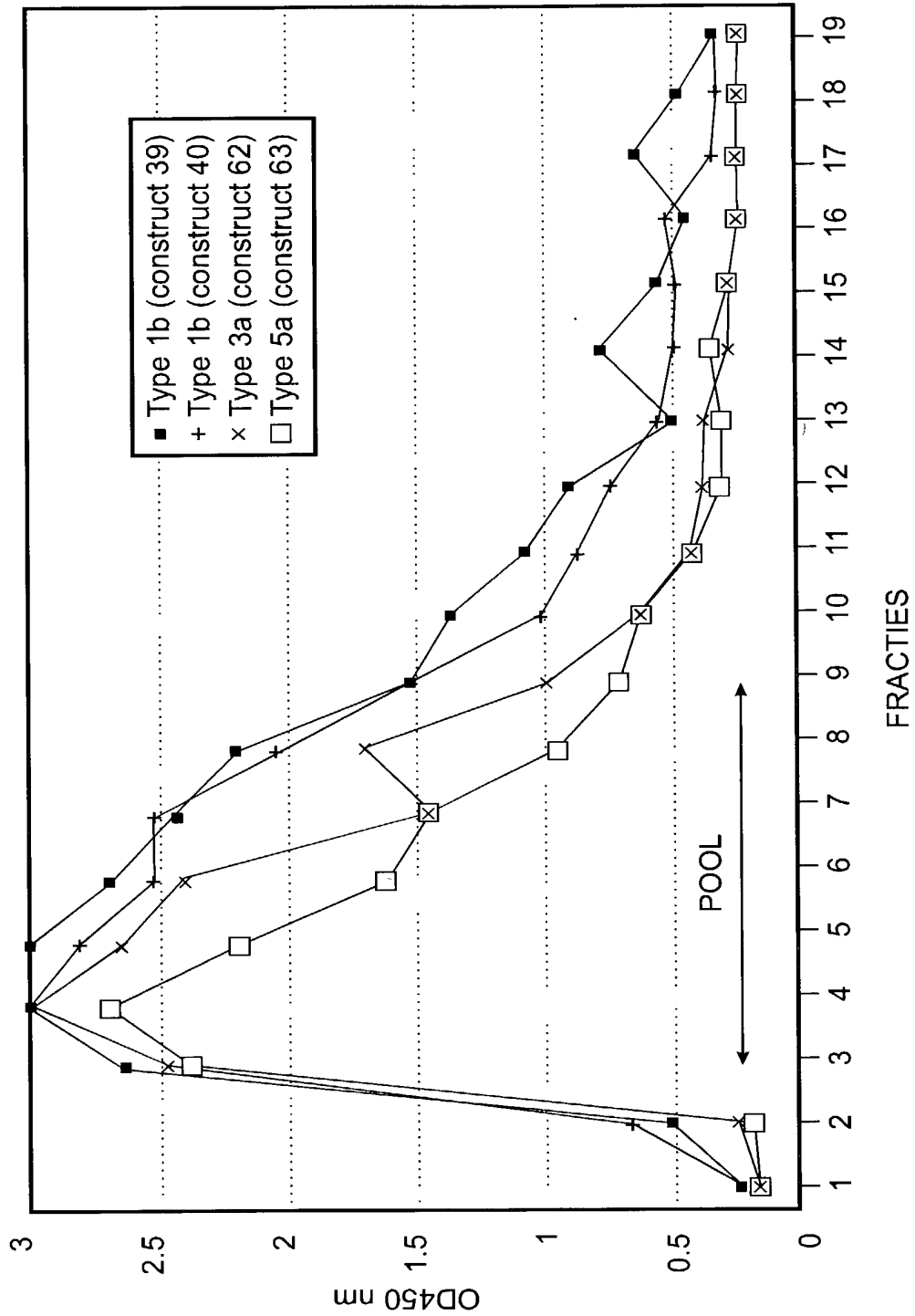


Figure 23





Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 33 of 64  
 Atty. Dkt.: 2551-69

OD measured at 450nm  
 construct

| Fraction | Volume | dilution | 39<br>type 1b | 40<br>type 1b | 62<br>type 3a | 63<br>type 5a |
|----------|--------|----------|---------------|---------------|---------------|---------------|
| 20       | 250µl  | 1/200    | 0.072         | 0.130         | 0.096         | 0.051         |
| 21       |        |          | 0.109         | 0.293         | 0.084         | 0.052         |
| 22       |        |          | 0.279         | 0.249         | 0.172         | 0.052         |
| 23       |        |          | 0.093         | 0.151         | 0.297         | 0.054         |
| 24       |        |          | 0.080         | 0.266         | 0.438         | 0.056         |
| 25       |        |          | 0.251         | 0.100         | 0.457         | 0.048         |
| 26       |        |          | 3             | 1.649         | 0.722         | 0.066         |
| 27       |        |          | 3             | 3             | 2.528         | 0.889         |
| 28       |        |          | 3             | 3             | 3             | 2.345         |
| 29       |        |          | 3             | 3             | 2.849         | 2.580         |
| 30       |        |          | 2.227         | 1.921         | 1.424         | 1.333         |
| 31       |        |          | 0.263         | 0.415         | 0.356         | 0.162         |
| 32       |        |          | 0.071         | 0.172         | 0.154         | 0.064         |
| 33       |        |          | 0.103         | 0.054         | 0.096         | 0.057         |
| 34       |        |          | 0.045         | 0.045         | 0.044         | 0.051         |
| 35       |        |          | 0.043         | 0.047         | 0.045         | 0.046         |
| 36       |        |          | 0.045         | 0.045         | 0.049         | 0.040         |
| 37       |        |          | 0.045         | 0.047         | 0.046         | 0.048         |
| 38       |        |          | 0.046         | 0.048         | 0.047         | 0.057         |
| 39       |        |          | 0.045         | 0.048         | 0.050         | 0.057         |
| 40       |        |          | 0.046         | 0.049         | 0.048         | 0.049         |

Figure 24



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 34 of 64  
Atty. Dkt.: 2551-69

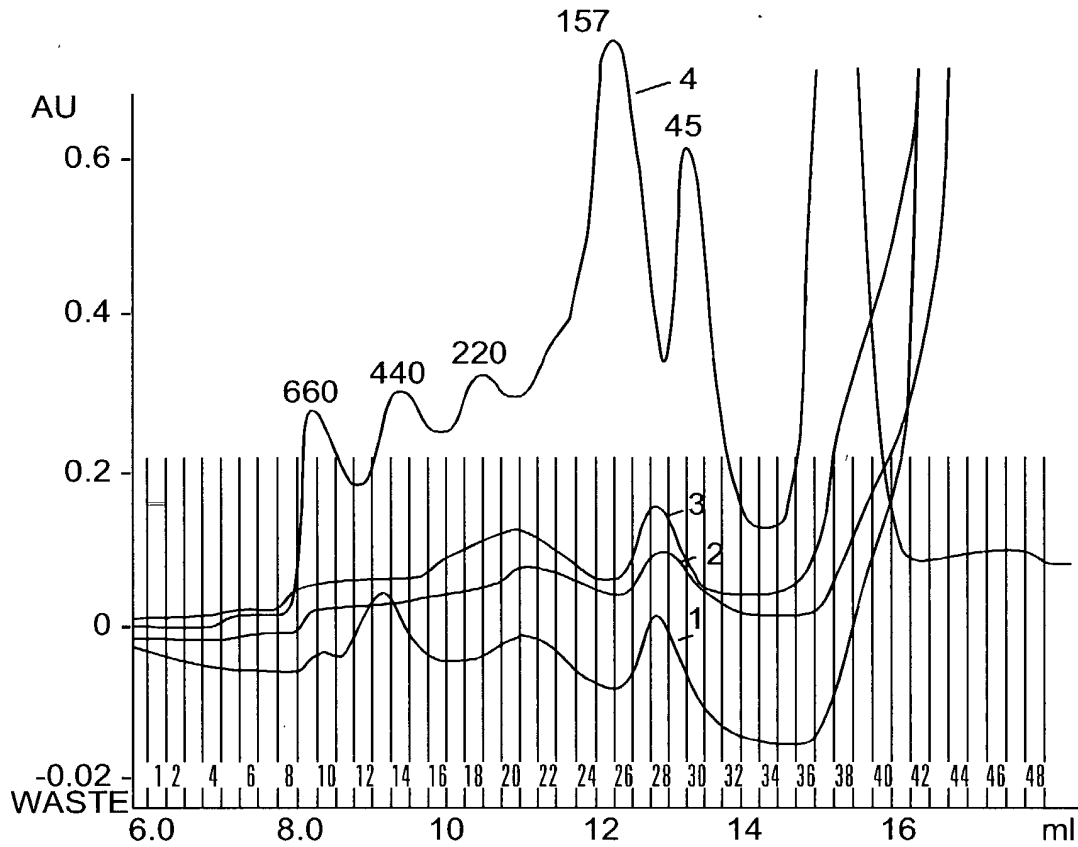


Figure 25



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 35 of 64  
Atty. Dkt.: 2551-69

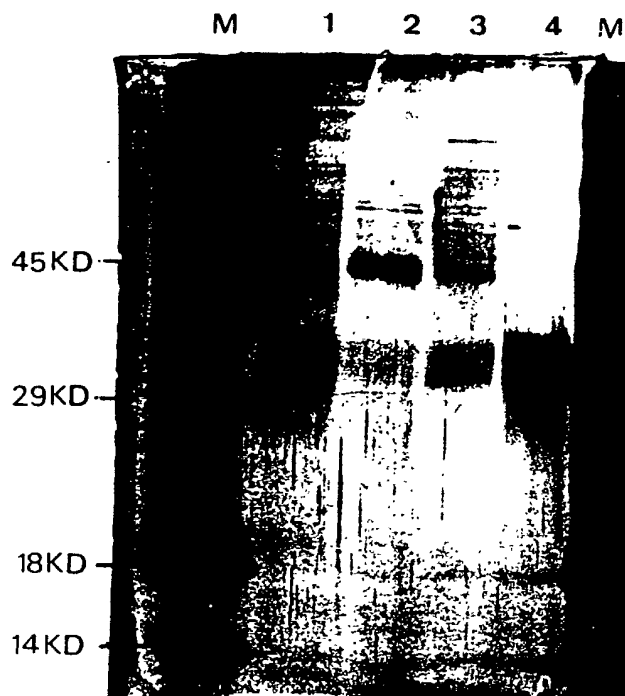


Fig. 26

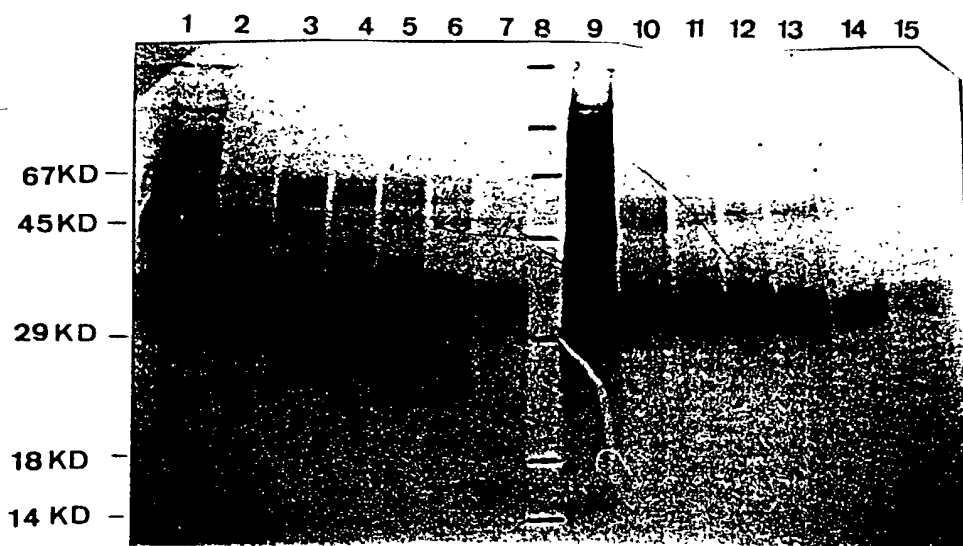


Fig. 27

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 36 of 64  
 Atty. Dkt.: 2551-69

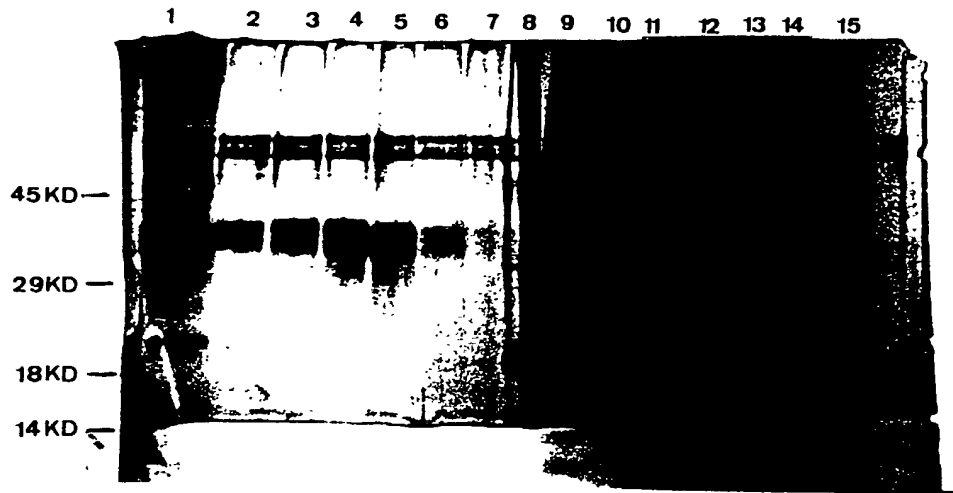


Fig.28

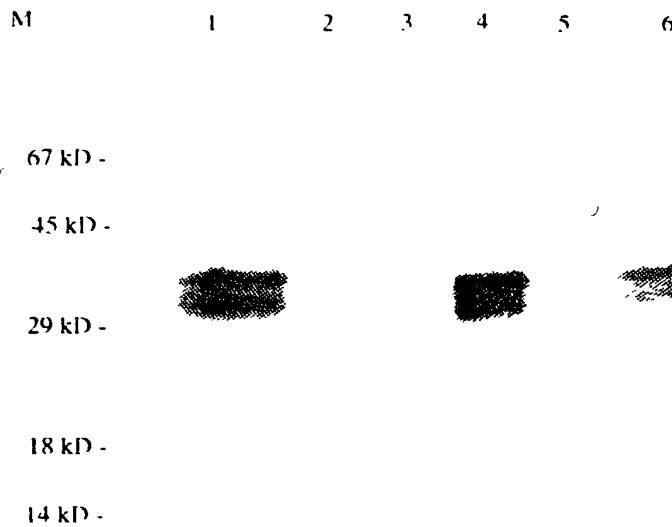


Fig.29

Lane 1: Crude Lysate  
 Lane 2: Flow through Lentil Chromatography  
 Lane 3: Wash with EMPIGEN Lentil Chromatography  
 Lane 4: Eluate Lentil Chromatography  
 Lane 5: Flow through during concentration lentil eluate  
 Lane 6: Pool of E1 after Size Exclusion Chromatography

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 37 of 64  
Atty. Dkt.: 2551-69

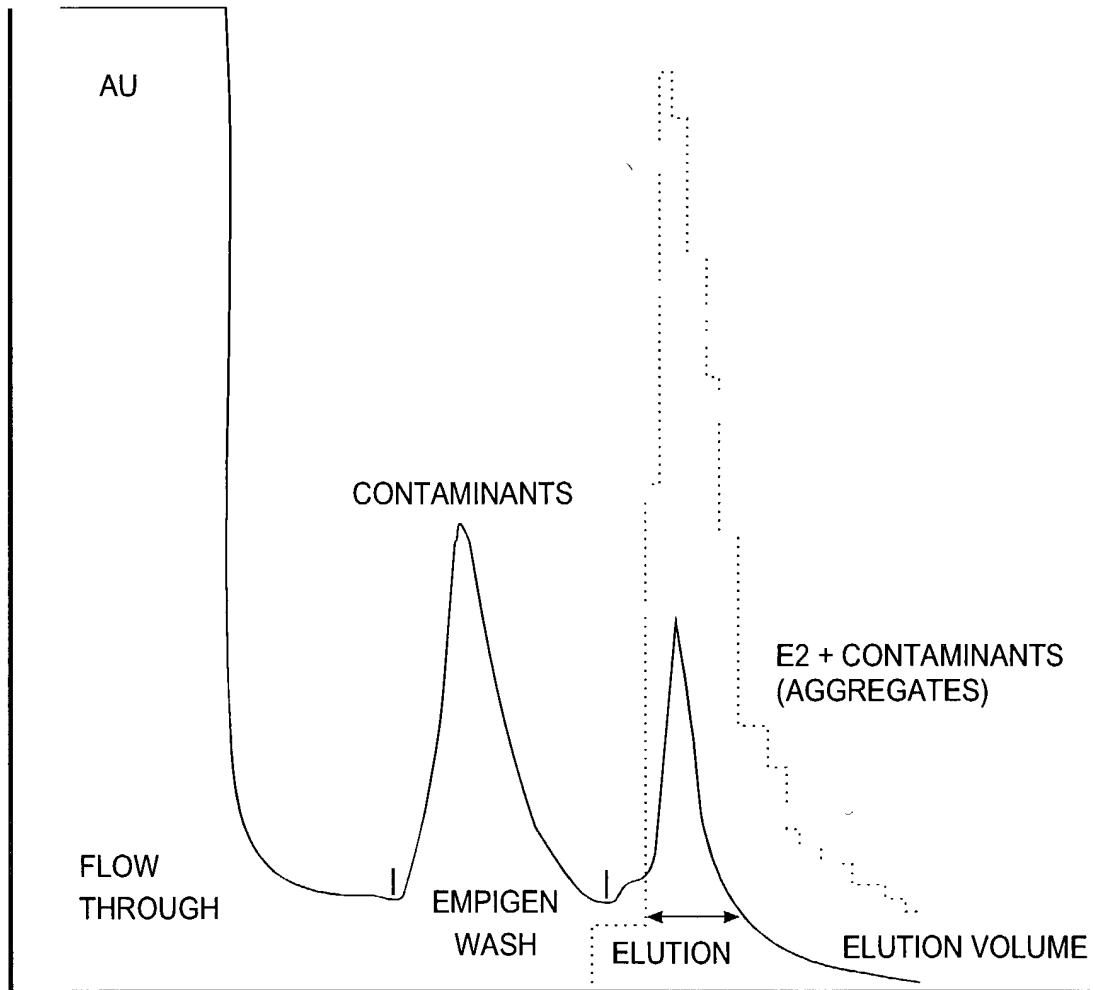


Figure 30

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 38 of 64  
Atty. Dkt.: 2551-69

NON-REDUCED

38 / 65

E2 + CONTAMINANTS (AGGREGATES)

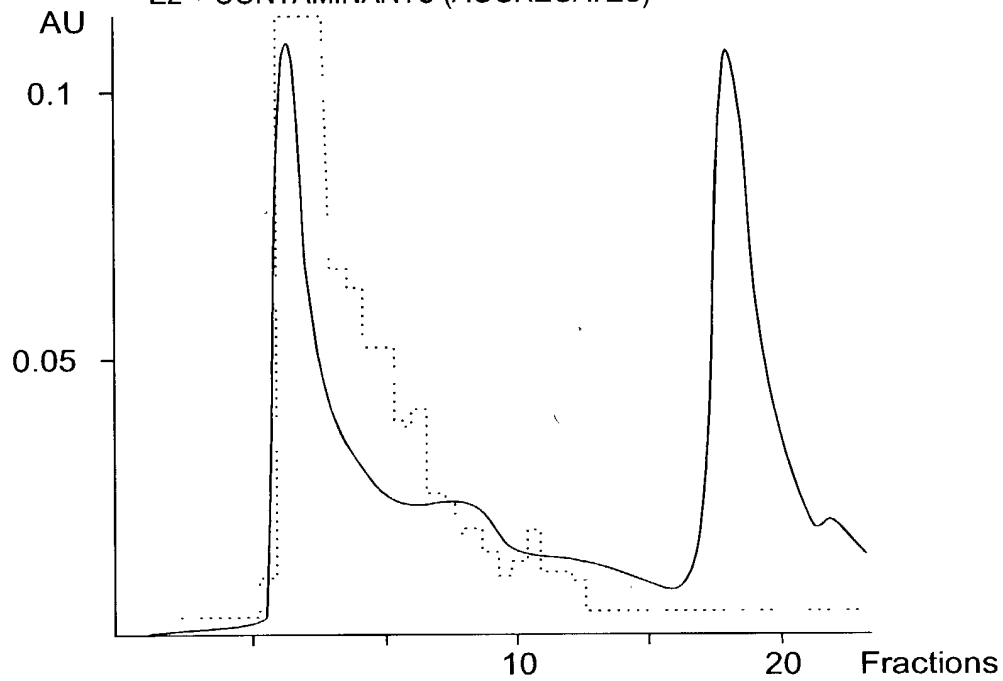


Figure 31A

REDUCED

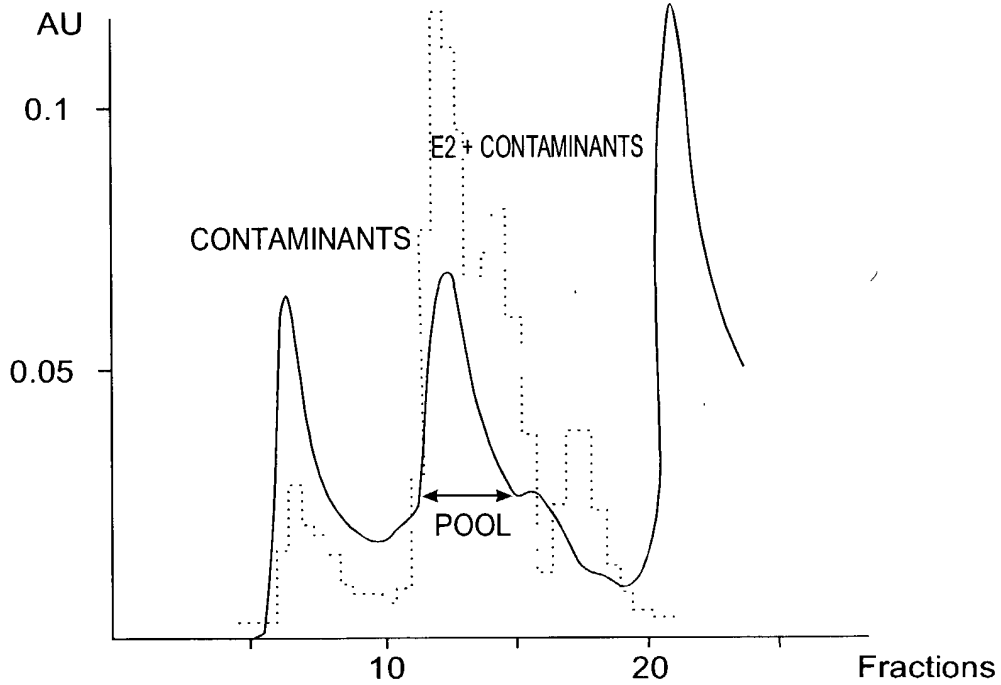


Figure 31B



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 39 of 64  
 Atty. Dkt.: 2551-69

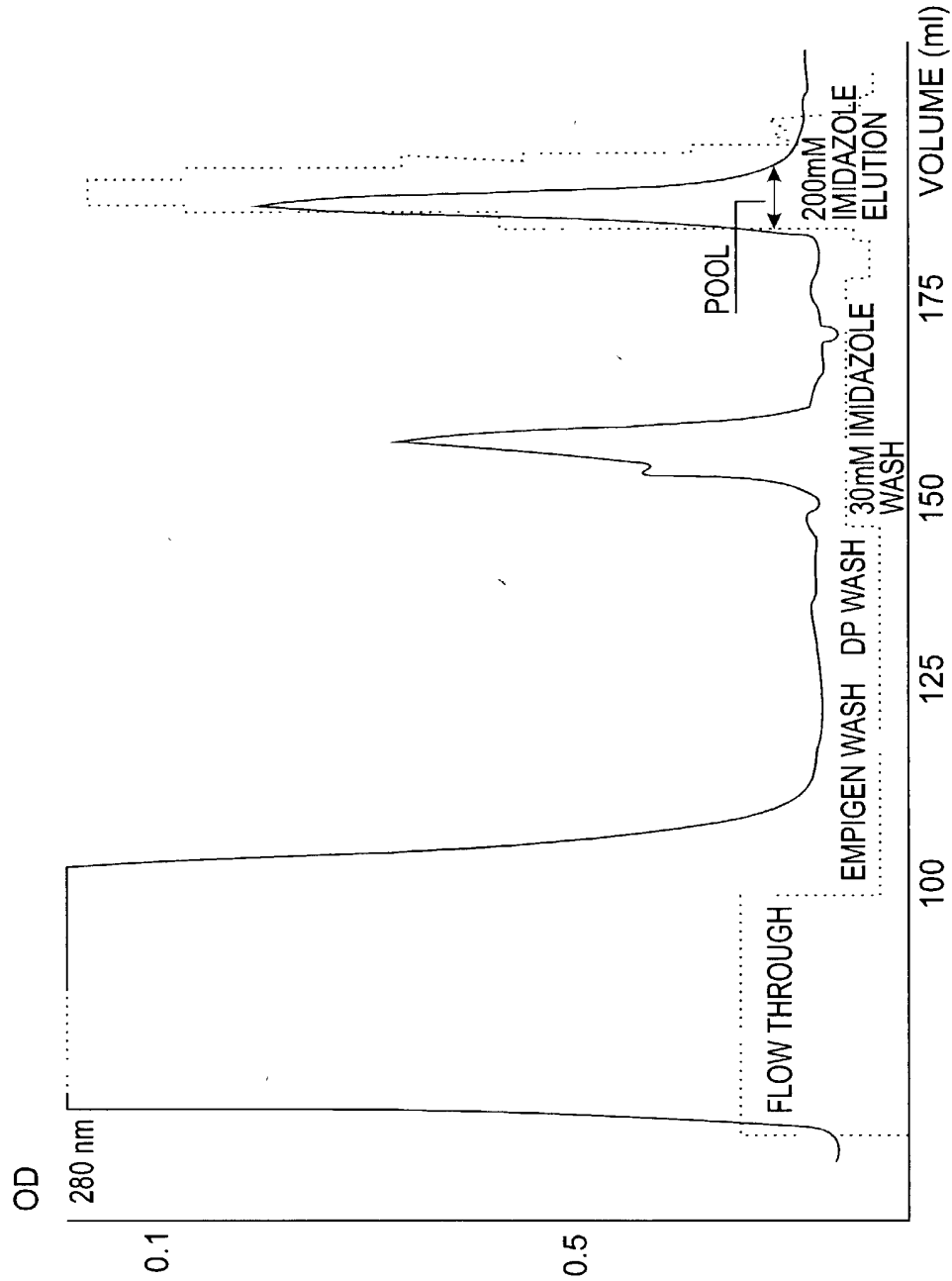
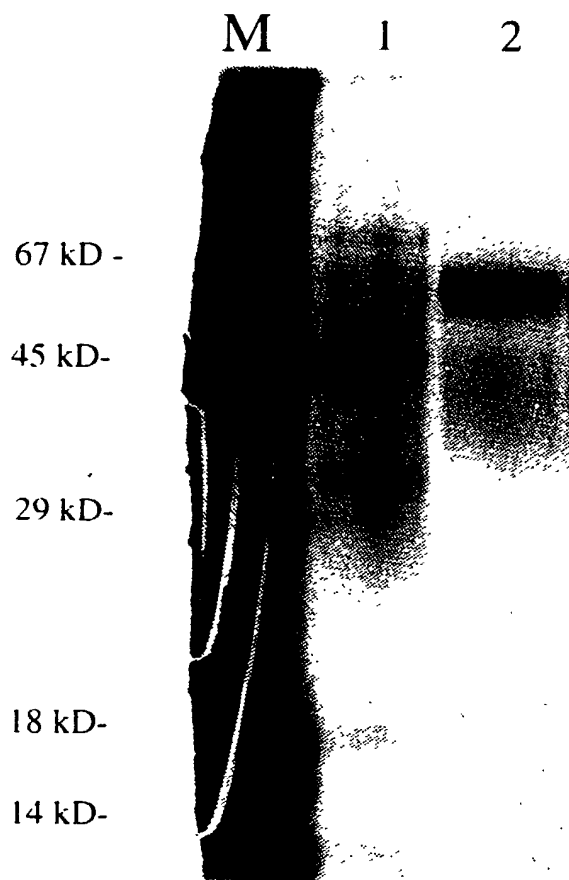


Figure 32

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 40 of 64  
Atty. Dkt.: 2551-69

## SILVER STAIN OF PURIFIED E2

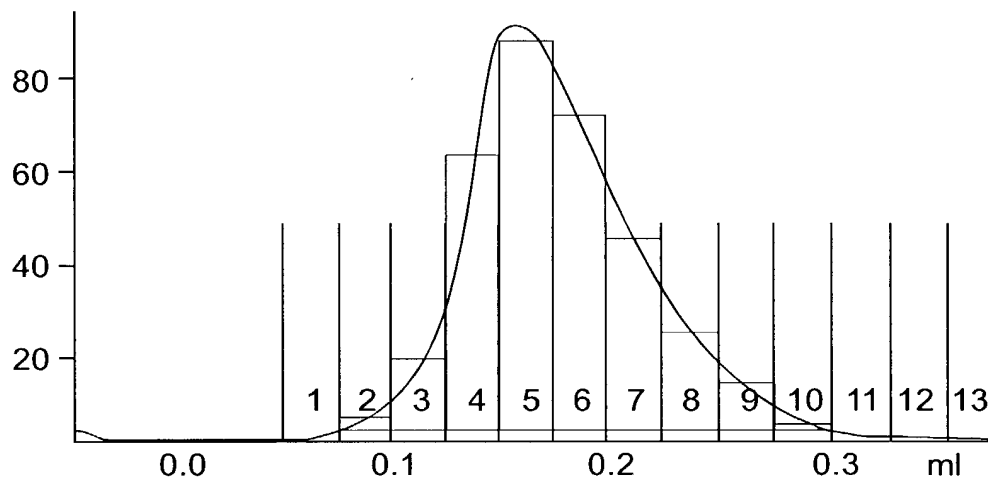


1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5 ug E2

Fig.33



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 41 of 64  
 Atty. Dkt.: 2551-69



| No. | Ret<br>(ml) | Peak start<br>(ml) | Peak end<br>(ml) | Dur<br>(ml) | Area<br>(ml*mAU) | Height<br>(mAU) |
|-----|-------------|--------------------|------------------|-------------|------------------|-----------------|
| 1   | -0.45       | -0.46              | -0.43            | 0.04        | 0.0976           | 4.579           |
| 2   | 1.55        | 0.75               | 3.26             | 2.51        | 796.4167         | 889.377         |
| 3   | 3.27        | 3.26               | 3.31             | 0.05        | 0.0067           | 0.224           |
| 4   | 3.33        | 3.32               | 3.33             | 0.02        | 0.0002           | 0.018           |

Total number of detected peaks = 4  
 Total Area above baseline = 0.796522 ml\*AU  
 Total area in evaluated peaks = 0.796521 ml\*AU  
 Ratio peak area / total area = 0.999999  
 Total peak duration = 2.613583 ml

Figure 34

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 42 of 64  
 Atty. Dkt.: 2551-69



NS4 Ab NR

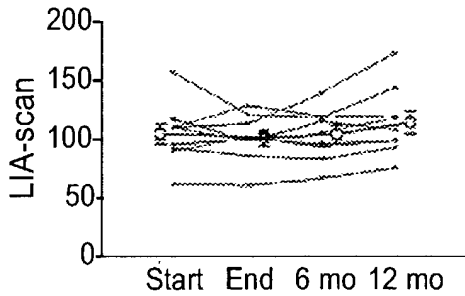


Fig. 35A-1

NS4 Ab LTR

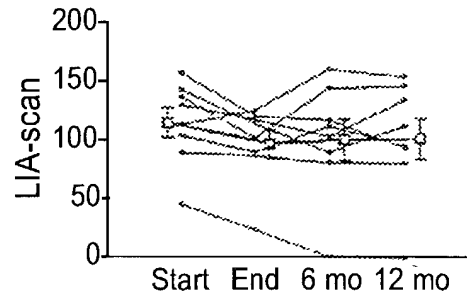


Fig. 35A-2

NS5 Ab NR

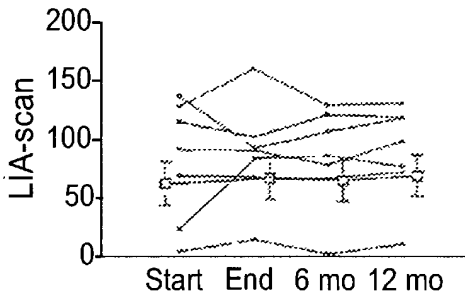


Fig. 35A-3

NS5 Ab LTR

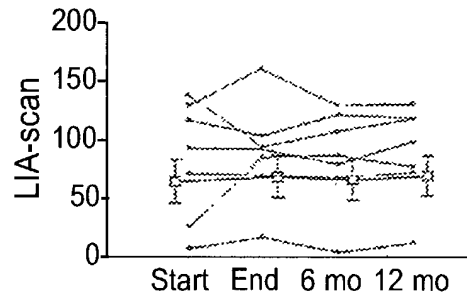


Fig. 35A-4

E1 Ab NR

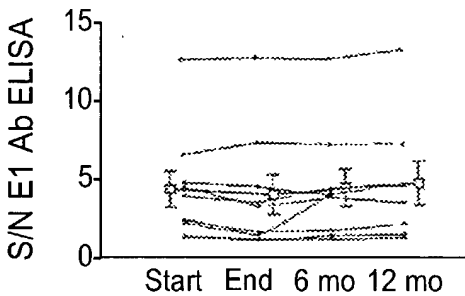


Fig. 35A-5

E1 Ab LTR

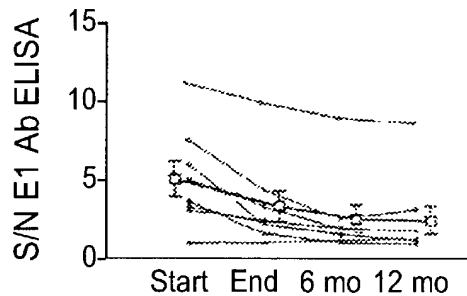


Fig. 35A-6

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 43 of 64  
Atty. Dkt.: 2551-69

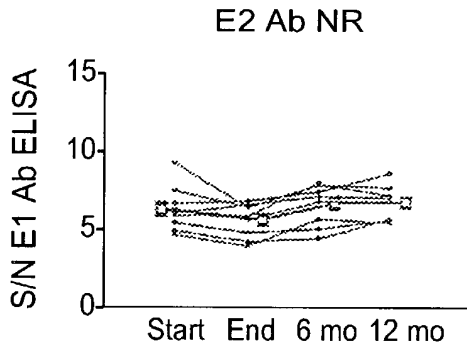


Fig. 35A-7

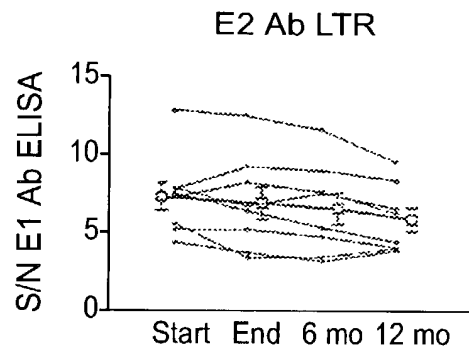


Fig. 35A-8



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 44 of 64  
 Atty. Dkt.: 2551-69

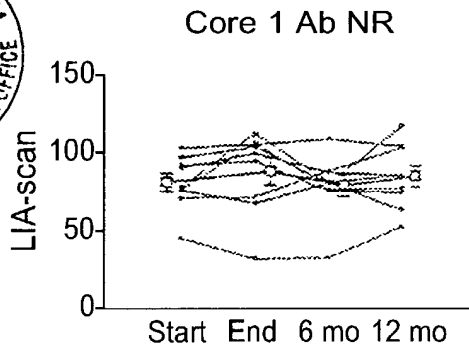


Fig. 35B-1

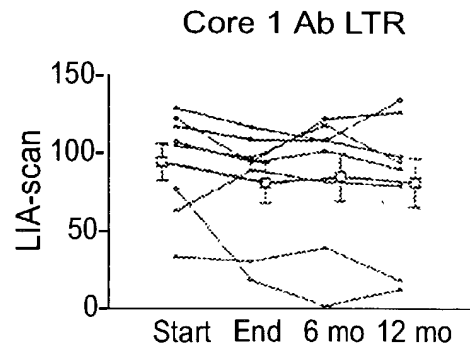


Fig. 35B-2

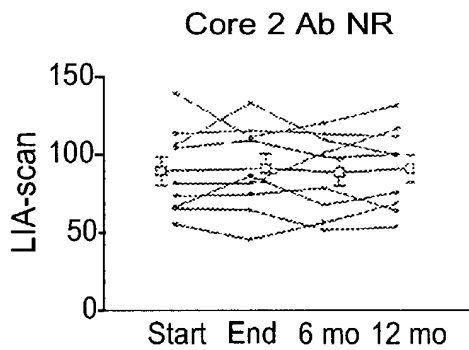


Fig. 35B-3

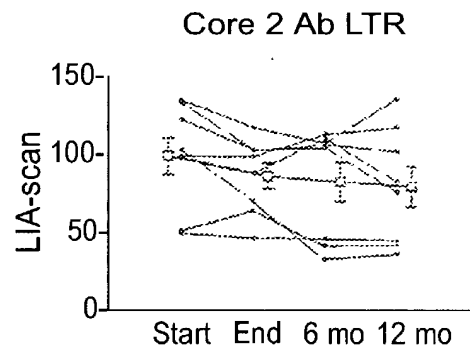


Fig. 35B-4

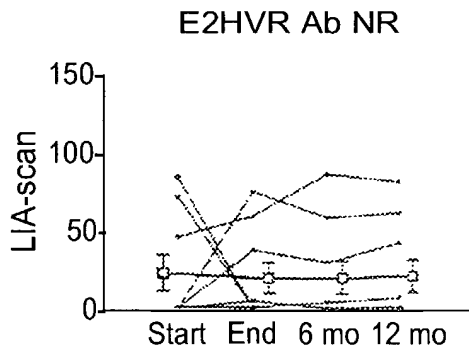


Fig. 35B-5

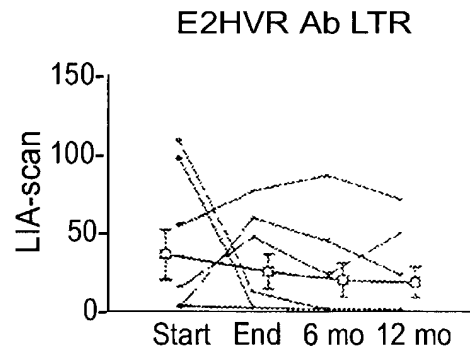


Fig. 35B-6

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 45 of 64  
Atty. Dkt.: 2551-69

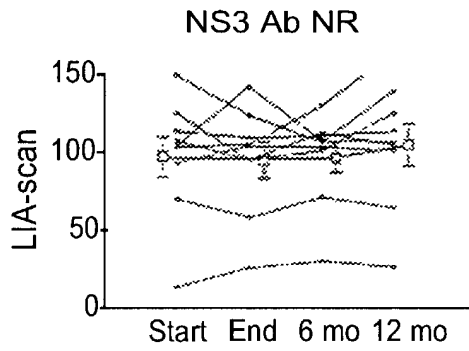


Fig. 35B-7

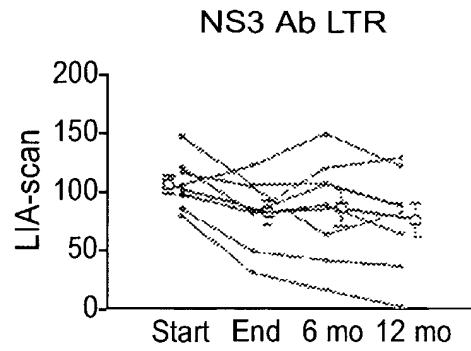


Fig. 35B-8

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 46 of 64  
Atty. Dkt.: 2551-69

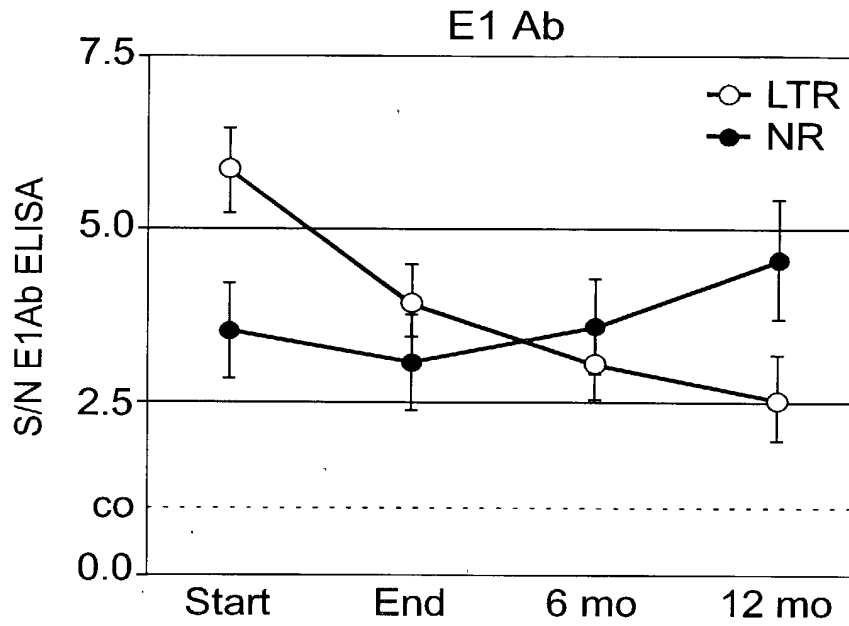
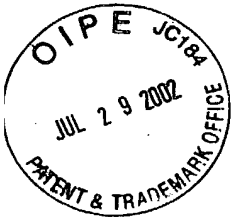


Figure 36A

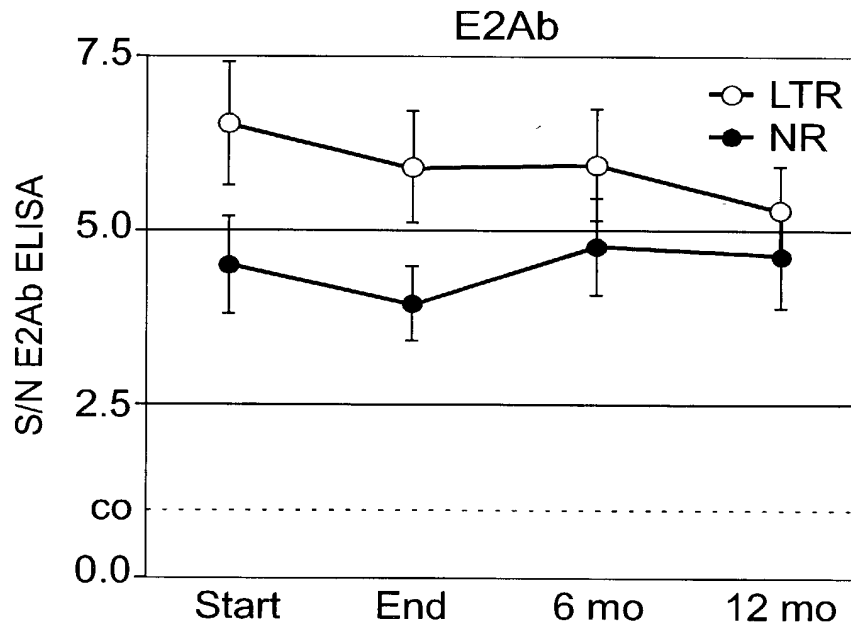


Figure 36B

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 47 of 64  
 Atty. Dkt.: 2551-69

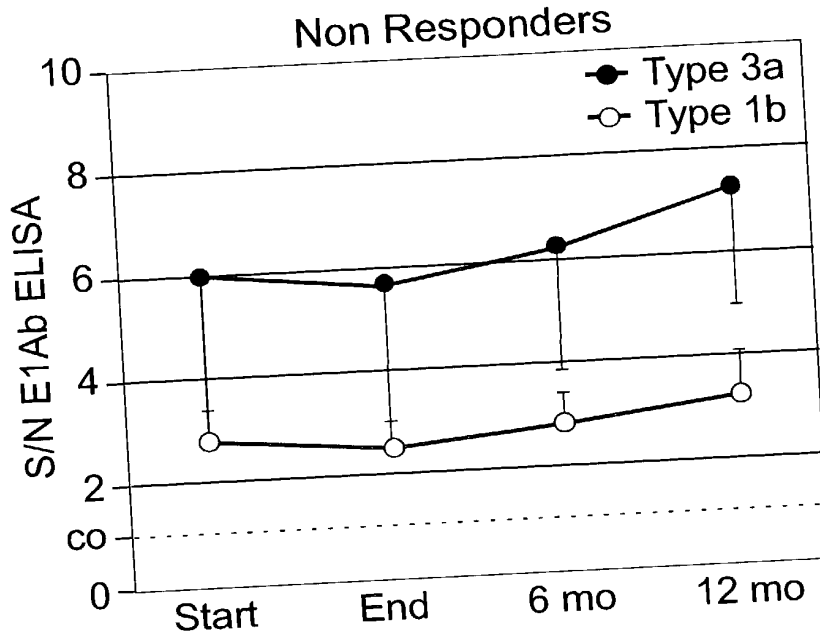


Figure 37A

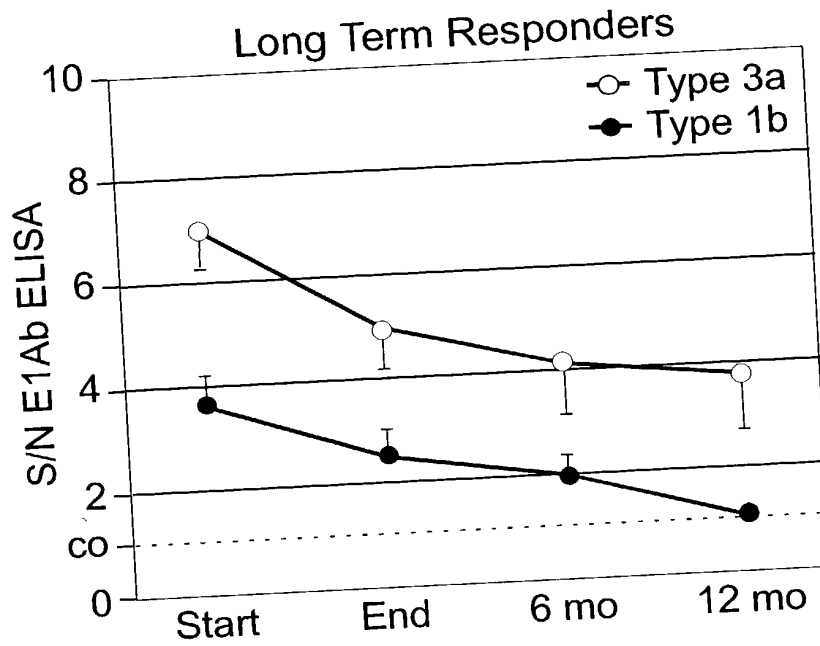


Figure 37B

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 48 of 64  
Atty. Dkt.: 2551-69

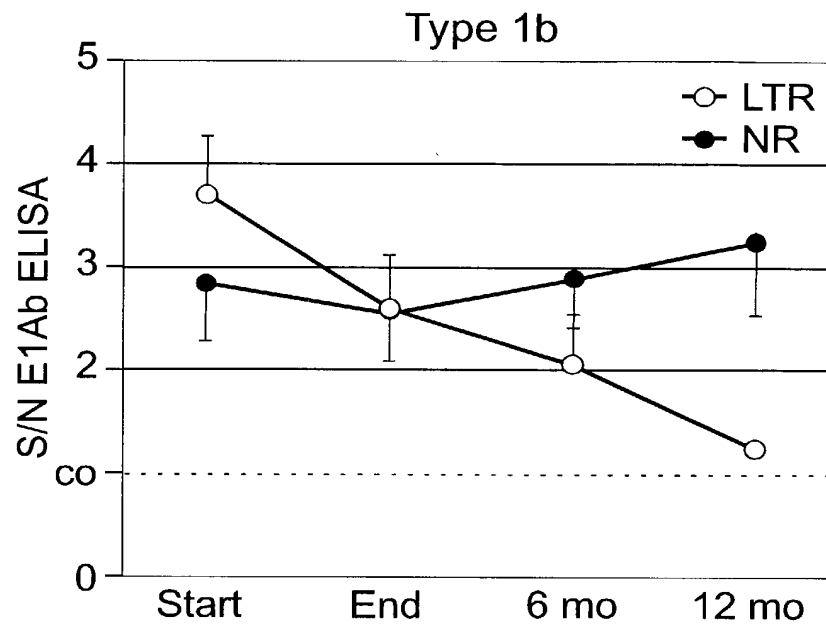


Figure 37C

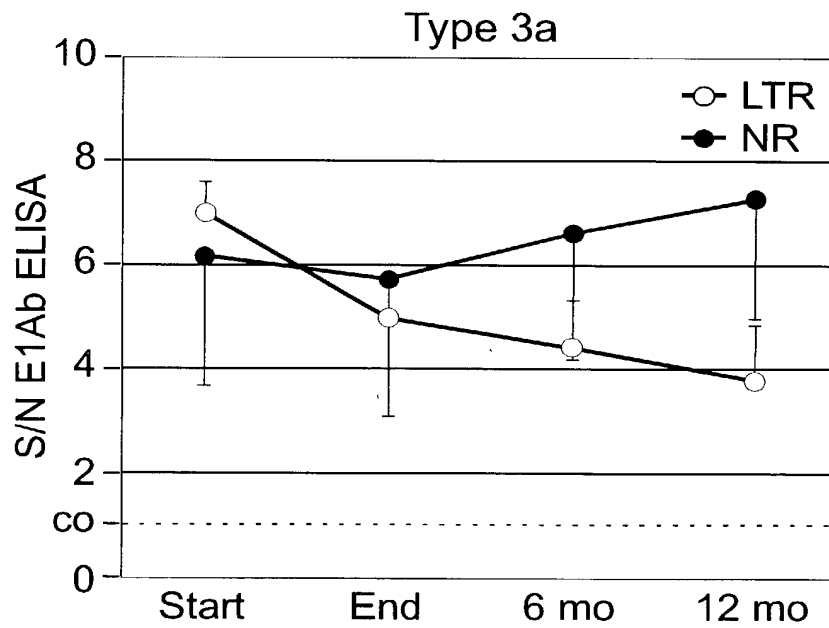


Figure 37D



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 49 of 64  
Atty. Dkt.: 2551-69



Relative Map Positions of  
anti-E2 monoclonal antibodies

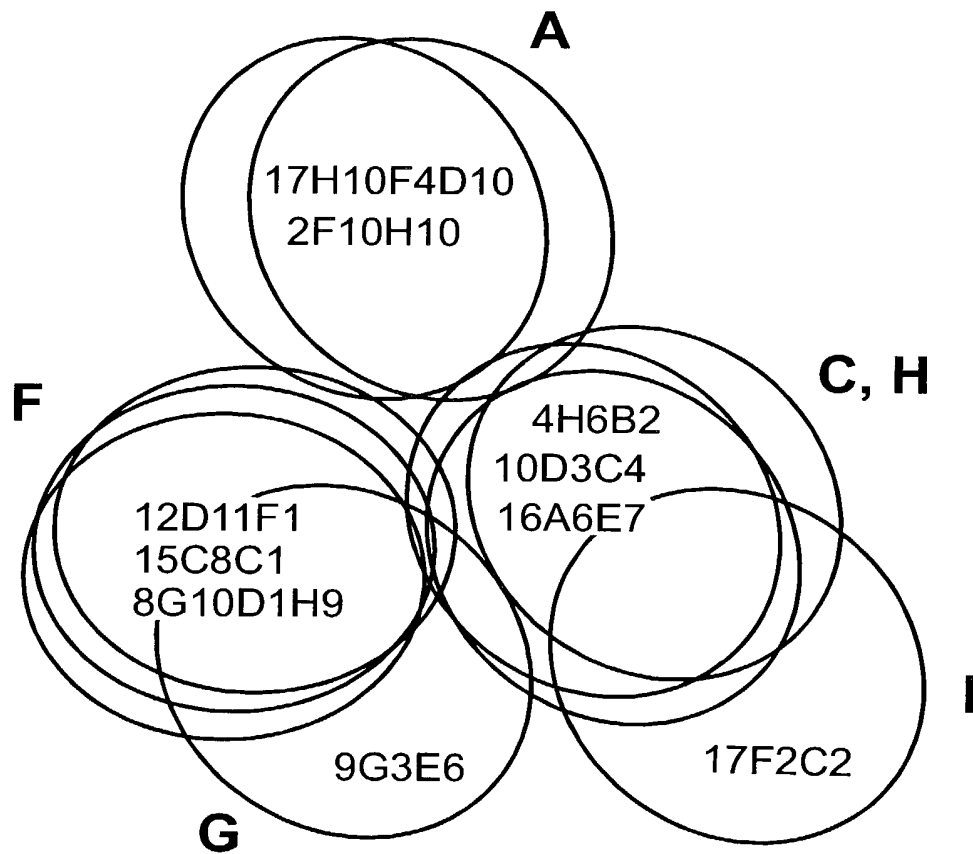


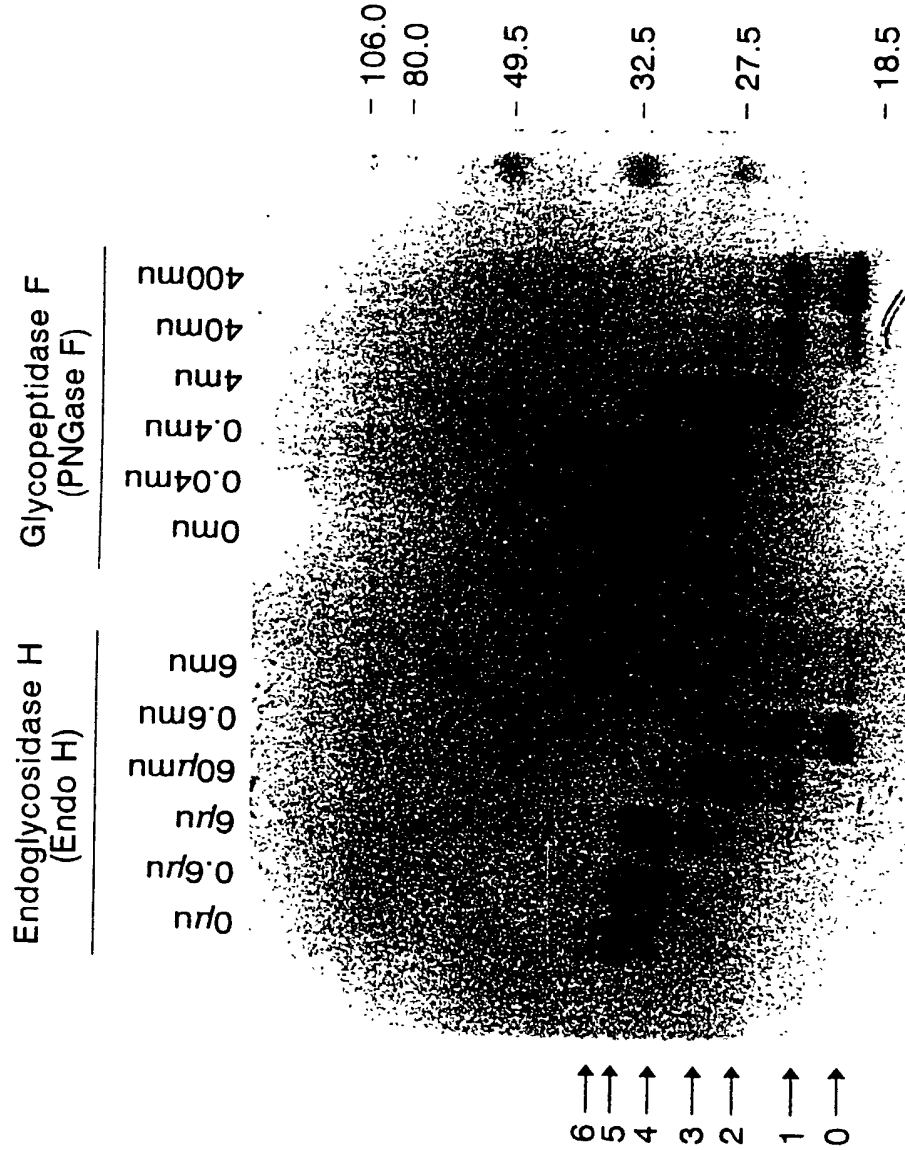
Figure 38

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 50 of 64  
 Atty. Dkt.: 2551-69



Fig.39

**PARTIAL DEGLYCOSYLATION  
 OF HCV E1 ENVELOPE PROTEIN**



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 51 of 64  
Atty. Dkt.: 2551-69



# PARTIAL TREATMENT OF HCV E2/E2s ENVELOPE PROTEINS BY PNGase F

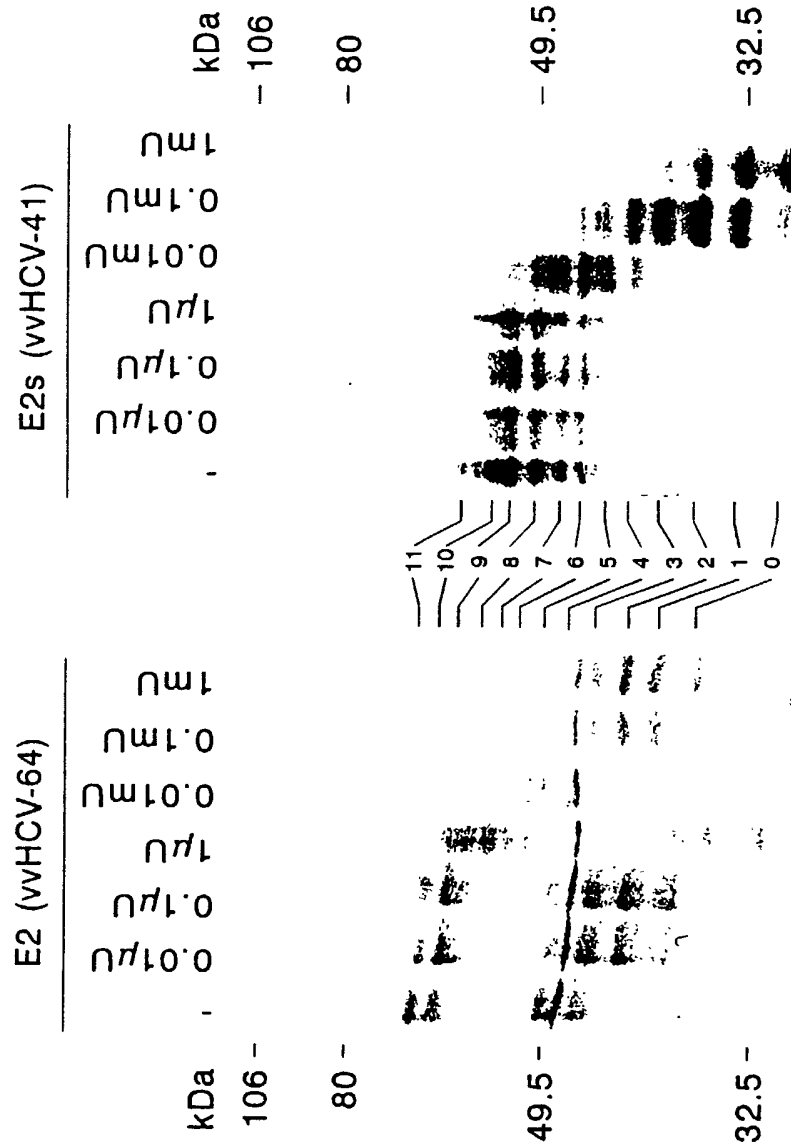


Fig. 40



09995860, 072982

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 52 of 64  
Atty. Dkt.: 2551-69

# In vitro mutagenesis of HCV E1 glycoprotein

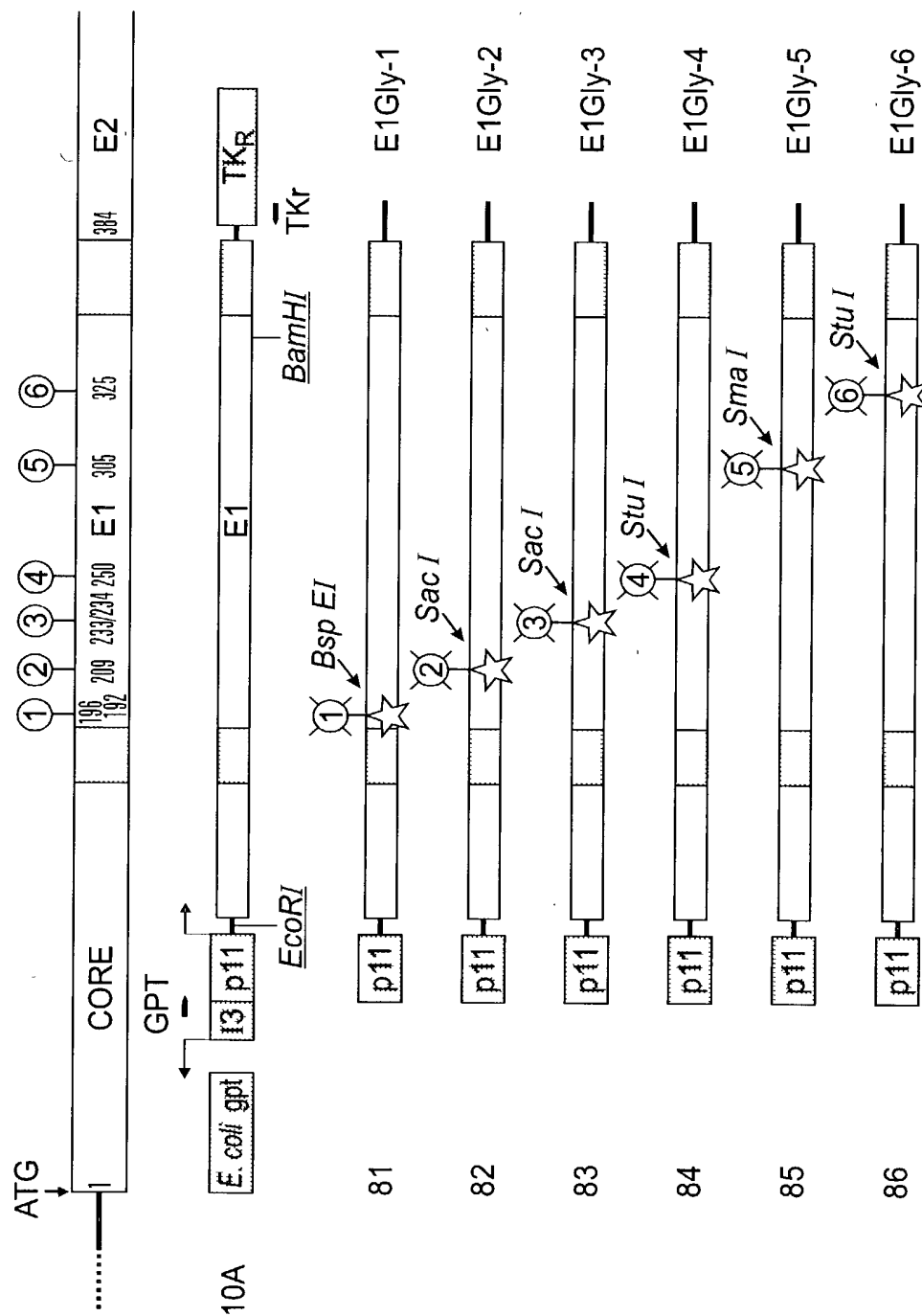


Figure 41



Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 53 of 64  
Atty. Dkt.: 2551-69

# In vitro mutagenesis of HCV E1 glycoprotein

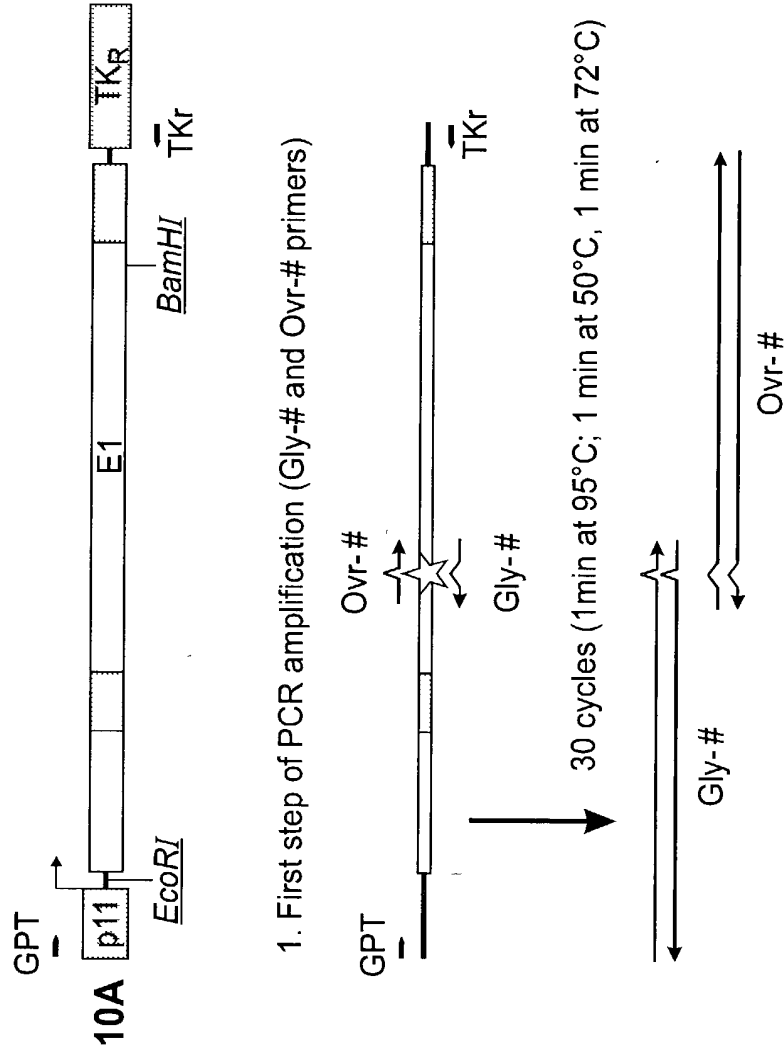


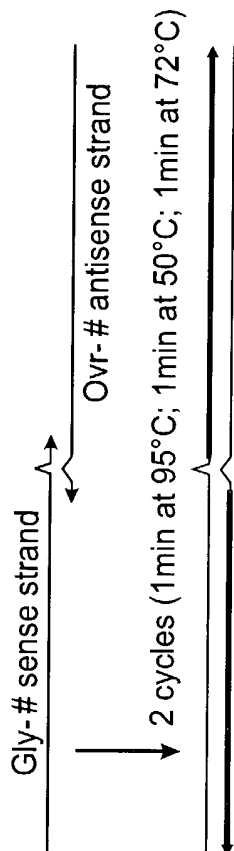
Figure 42A

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 54 of 64  
 Atty. Dkt.: 2551-69



## 2. Overlap extension and nested PCR

### a. Overlap extension



### b. Nested PCR amplification (GPT-2 and TKr-2 primers)

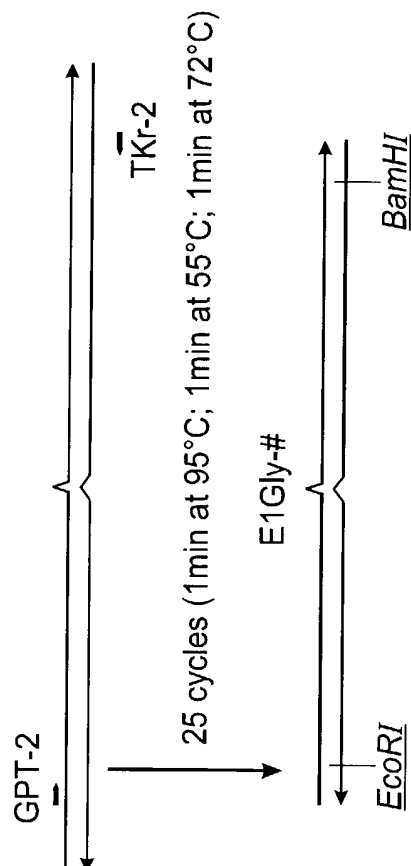


Figure 42B



# In vitro mutagenesis of HCV E1 glycoprotein

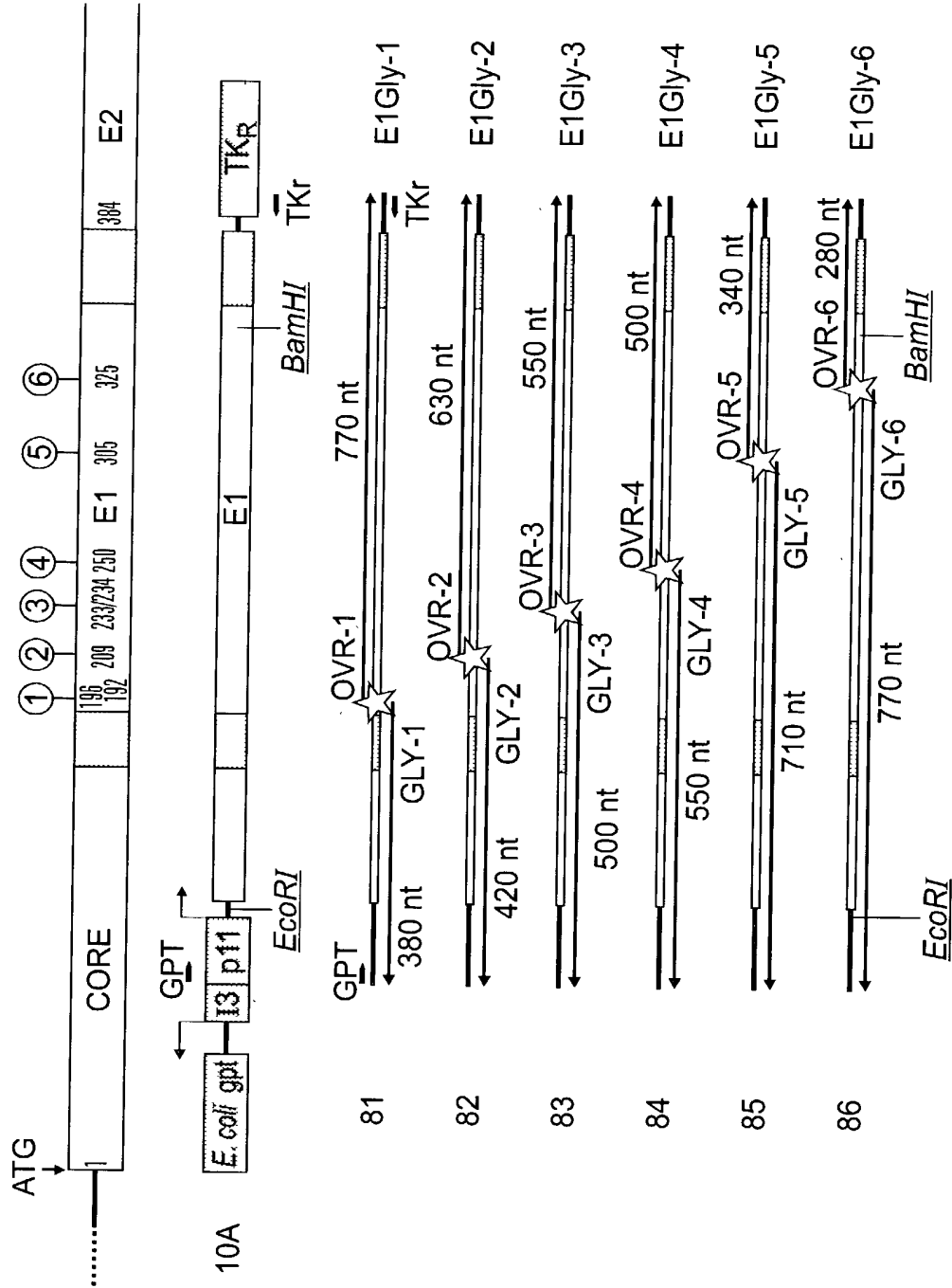


Figure 43

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 55 of 64  
Atty. Dkt.: 2551-69

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 56 of 64  
Atty. Dkt.: 2551-69

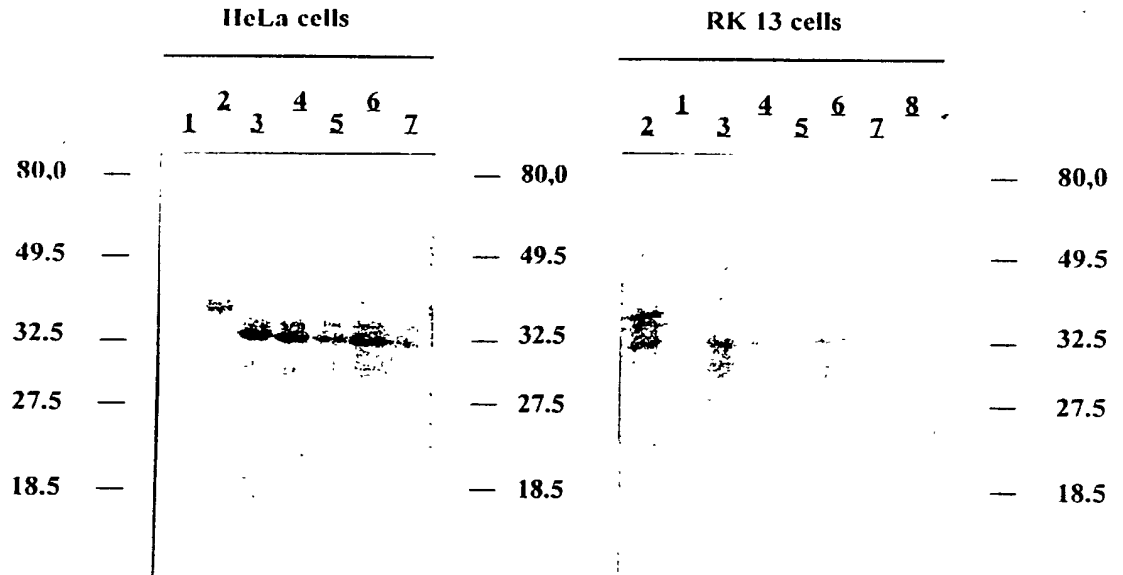


Fig. 44A

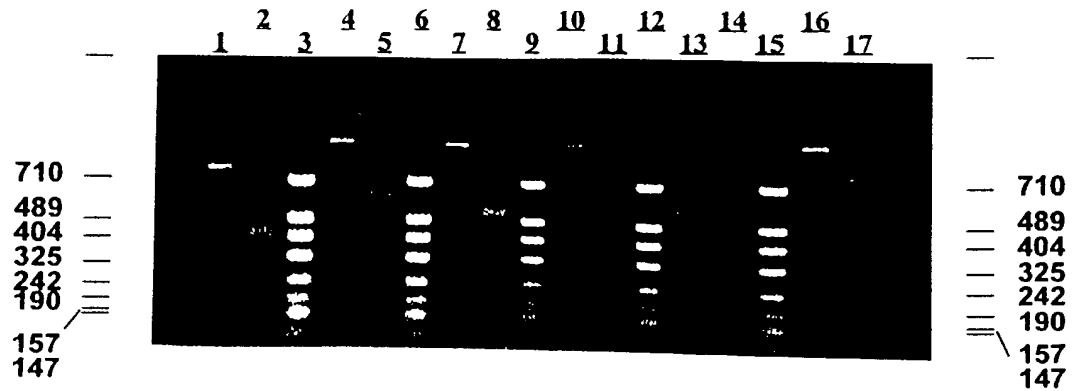


Fig. 44B



Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 57 of 64  
 Atty. Dkt.: 2551-69

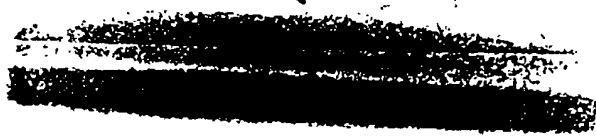


Fig.45

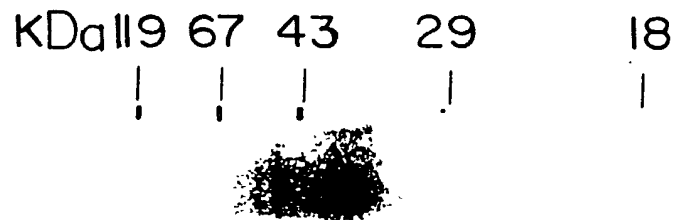


Fig.46

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 58 of 64  
 Atty. Dkt.: 2551-69



|        | age<br>(years) | HCV infection<br>(years) | genotype |
|--------|----------------|--------------------------|----------|
| Marcel | 17             | 9                        | 1a       |
| Peggy  | 21             | 16,5                     | 1b       |
| Femma  | 15             | 9                        | 1a       |
| Yoran  | 12             | none                     |          |
| Marti  | 12             | none                     |          |

**chronic carriers (strong T-cell adjuvant)**

↓ ↓ ↓ ↓ ↓ ↓      ↓ ↓ ↓ ↓ ↓ ↓      50 µg E1 dose

0 3 6 9 12 15      26 29 32 35 38 41      weeks

**naive (alum)**

↓ ↓ ↓ ↓ ↓ ↓      50 µg E1 dose

0 3 6 9 12 15      weeks

Figure 47

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 59 of 64  
 Atty. Dkt.: 2551-69

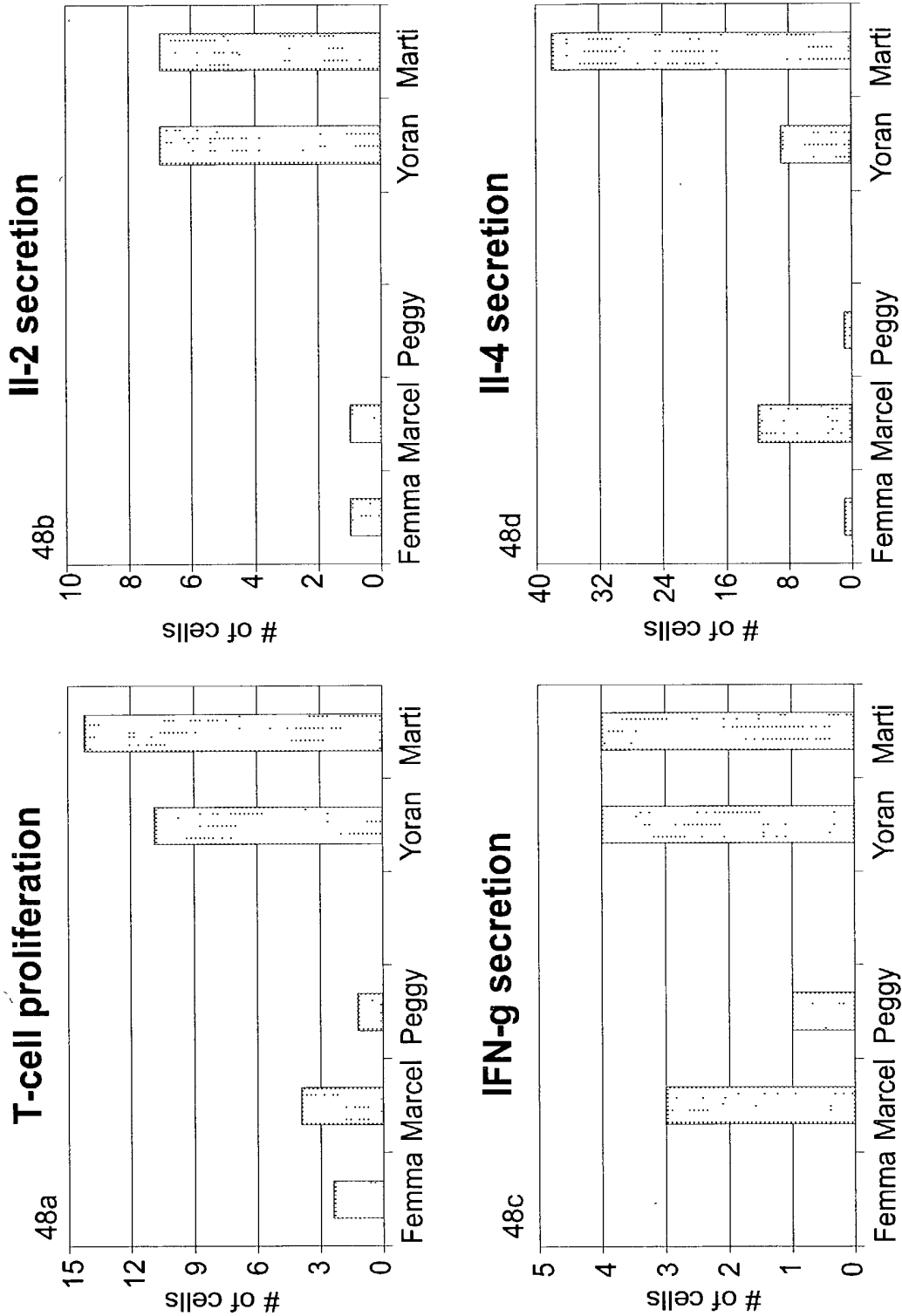
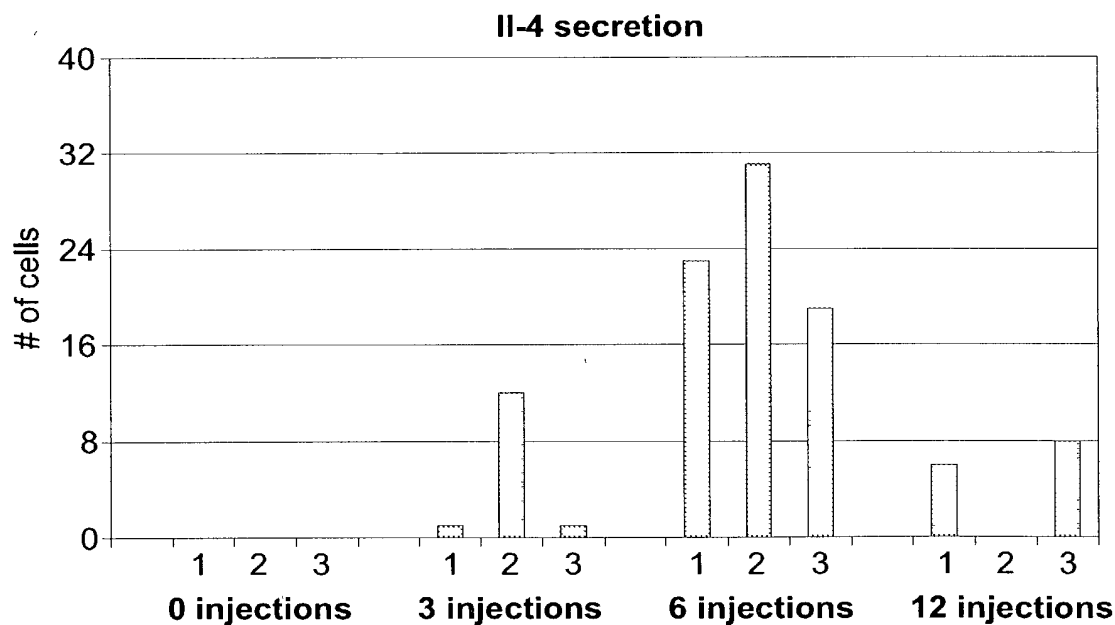
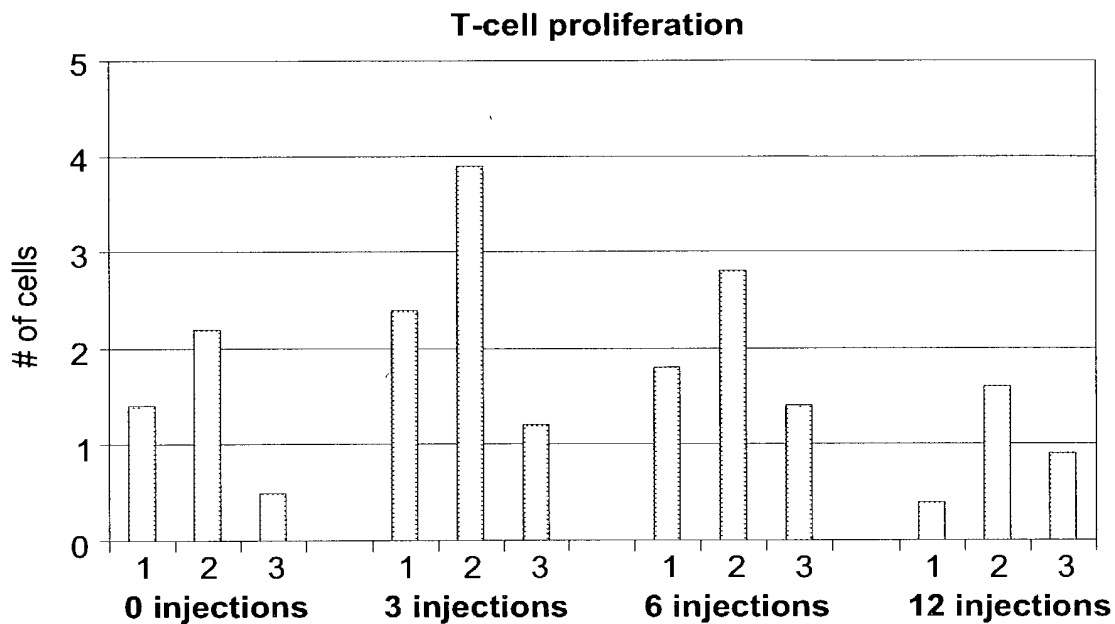


Figure 48

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 60 of 64  
Atty. Dkt.: 2551-69



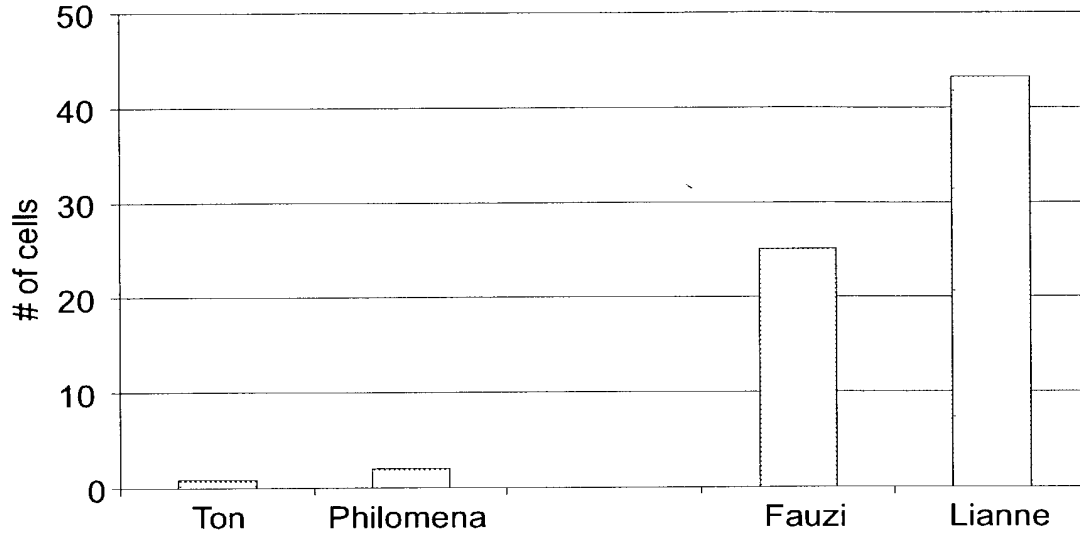
1: Femma, 2: Marcel, 3: Peggy

Figure 49

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 61 of 64  
Atty. Dkt.: 2551-69



### T-cell proliferation



### IL-2 secretion

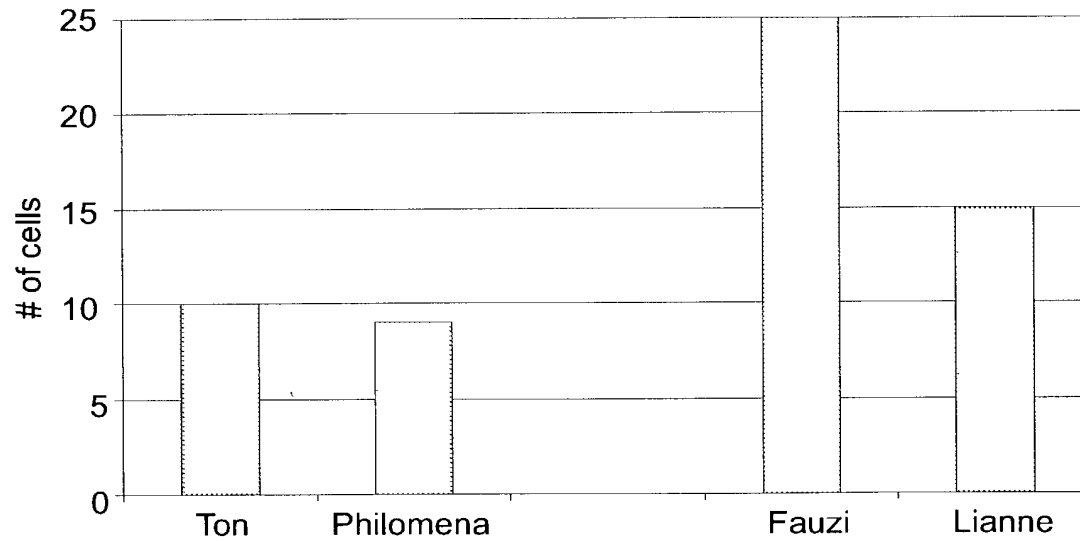


Figure 50

Inventor: MAERTENS, et al.  
 SN 09/995,860/Sheet 62 of 64  
 Atty. Dkt.: 2551-69

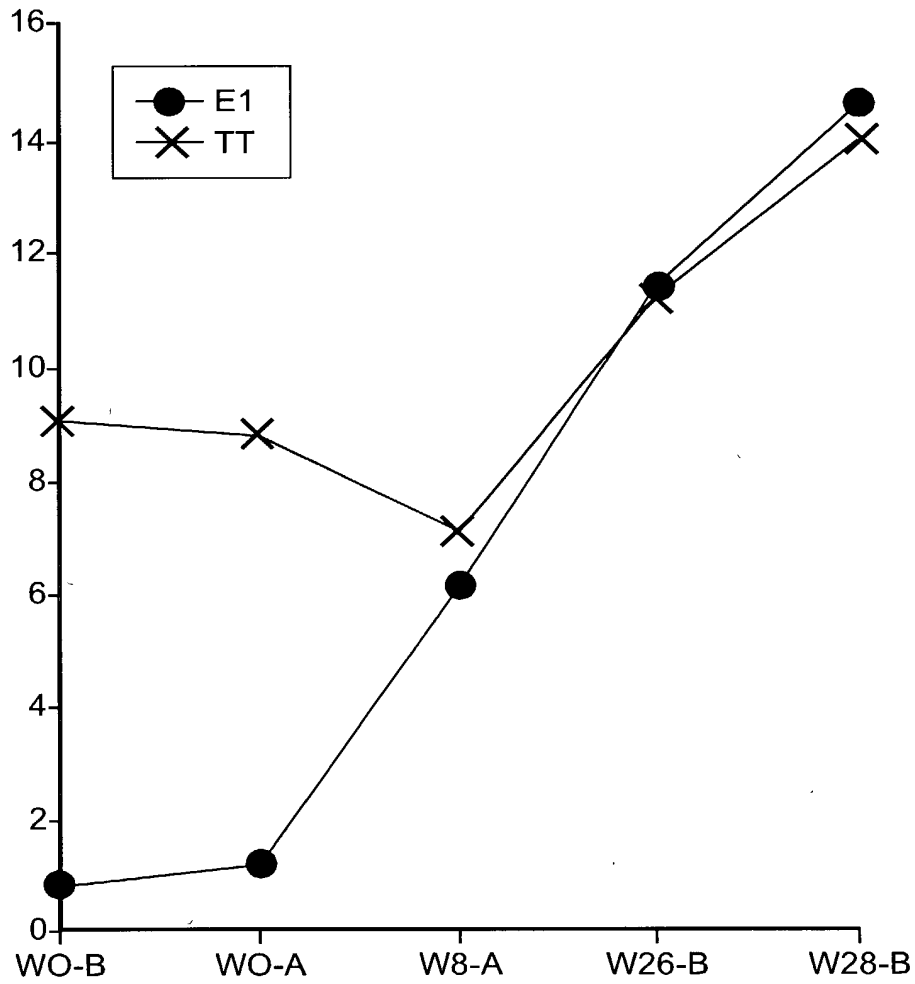


Figure 51

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 63 of 64  
Atty. Dkt.: 2551-69

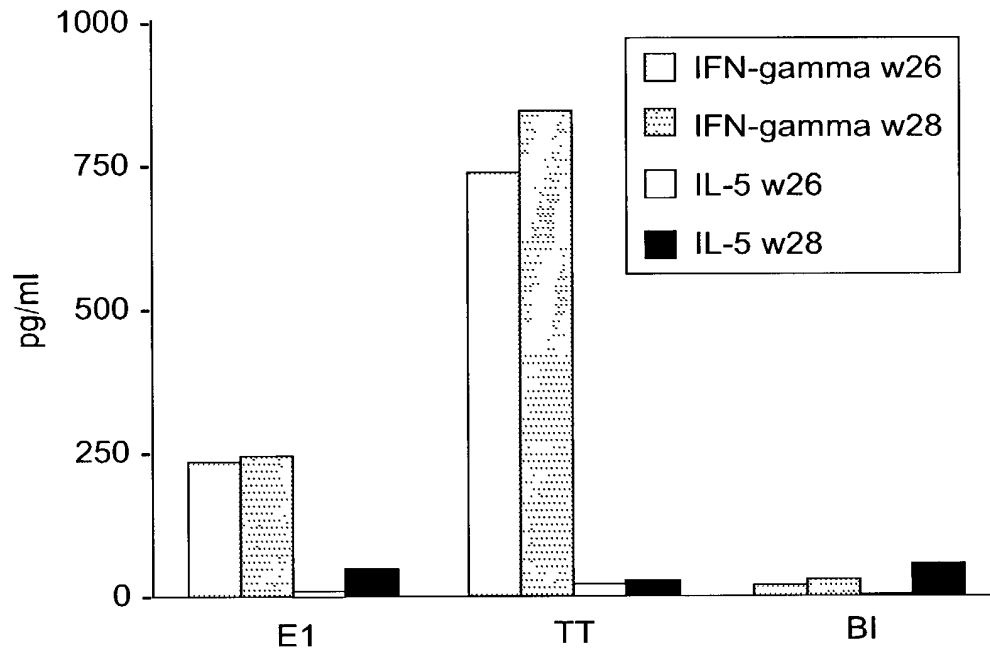


Figure 52

Inventor: MAERTENS, et al.  
SN 09/995,860/Sheet 64 of 64  
Atty. Dkt.: 2551-69

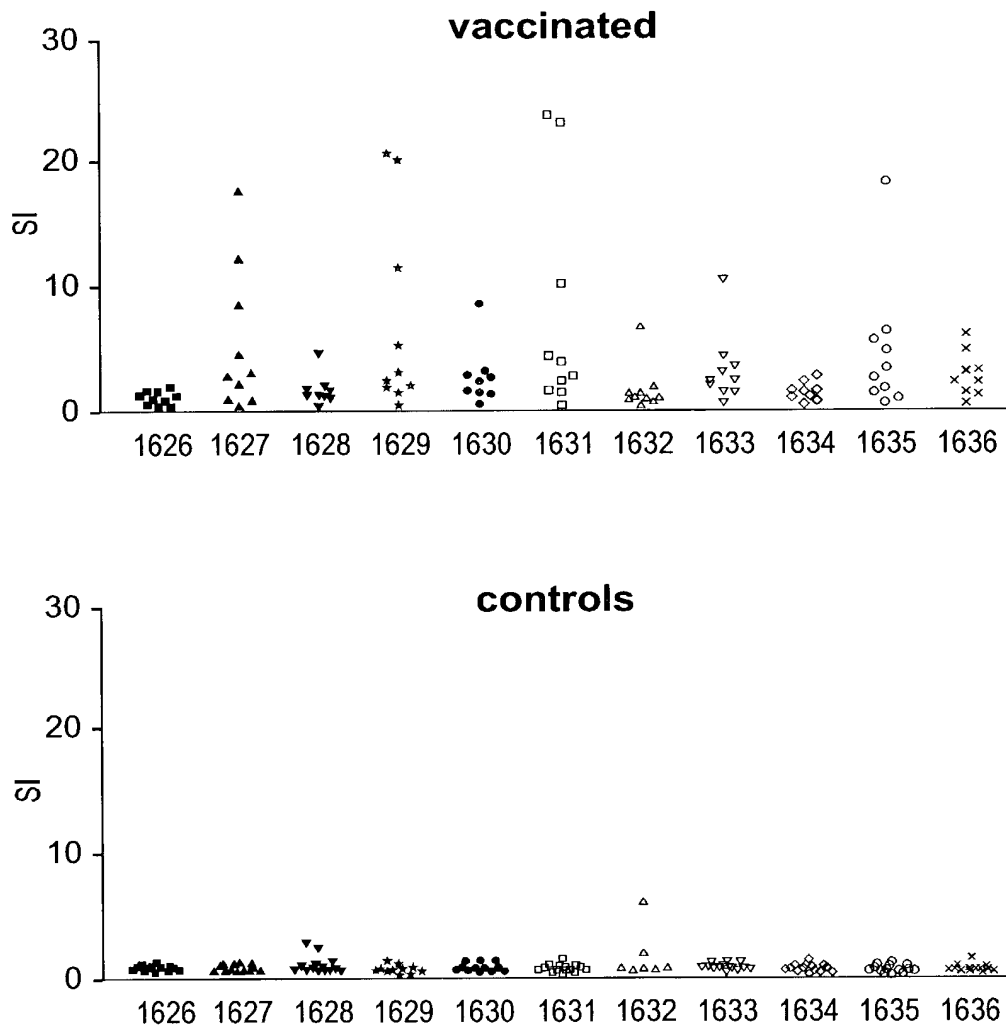


Figure 53